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PRESENT DAY TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS

THE MINOT LECTURE

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In the first Minot lecture, Dr. Castle [1] reviewed and commented on the contributions of Dr. Minot to the field of experimental medicine. In the second Minot lecture, Dr. Sturgis [2] summed up the information concerning a subject that was of lifelong interest to Dr. Minot, namely, leukemia. It was through a patient with a disorder of the blood coagulating mechanism, purpura hemorrhagica, that I met Dr. Minot for the first time. He visited Baltimore late in the autumn of 1923, and my colleague Dr. A. R. Felty and I had the opportunity of discussing with him the illness of the patient who, although she had had acute purpura hemorrhagica from which she recovered spontaneously, had remained well for several months without relapse. It was at that time that I learned of Dr. Minot's deep interest in the broad field of hematology and scientific medicine. Later, as a member of his staff at the Thorndike Memorial Laboratory, I came to appreciate Dr. Minot's contributions to experimental medicine and therapeutics and his example of university medical ideals.

The fact that this section is called experimental medicine and therapeutics is a conspicuous recognition of the fact that the practice of medicine is founded on the experimental method. There is no denying that it is from experiment and a search for the truth that scientific advances are made. Also, no thoughtful person will deny that medical progress during the first half of this century has stemmed primarily from the accumulation of scientific knowledge and its application to the prevention of disease and to the care of the sick through improved medical education and public health practice. Certainly, the central core of a better understanding of the sick stems from the advancement of knowledge and its transmission by our university medical schools. Dr. Minot was a physician who was educated in the basic medical sciences and one who practiced the university medical educational ideal. Through experiment, through the furtherance of knowledge, and through its translation to patients he added much. Dr. Minot learned how to apply the facts of fundamental science that were of practical benefit to the sick. For these reasons, I want to discuss a disease that serves as an example of what can be learned through experimental medicine over a period of 100 years to lead to a partial solution to the problem. I refer to bacterial endocarditis.

Within recent years, it has been found that in many cases bacterial endocarditis, like many other bacterial infections, can be treated successfully. This is especially true of that form of bacterial endocarditis commonly known as subacute bacterial endocarditis caused by Streptococcus viridans or one of the related nonhemolytic streptococci.

RESULTS BEFORE ADEQUATE THERAPY

Before the active therapeutic age, patients with bacterial endocarditis fell into four major groups: first, those in whom the disease was active, with or without bacteremia, and in whom death occurred within 4 to 18 months after the onset of symptoms and signs of infection. This group comprised about 97% of all cases. Second, there was a small group of patients who recovered from the active infection of the heart valves but who died subsequently from the sequellae of the infection, that is, from heart failure, chronic nephritis, or embolism. These patients usually died within one to three years after signs of active infection disappeared. Third, there was a small group of patients who recovered from the infection and remained well for many years without symptoms. Fourth, there was a group of patients in whom there was an arrest of the infection but in whom signs of either recurrence or reinfection developed at a later date; these died of active infection.

These four groups are seen today, but their distribution is quite different. More and more patients recover from the acute infection, but other problems remain. In order to develop better methods of treatment and to

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1. Castle, W. B.: The Contributions of George Richards Minot to Experimental Medicine (George R. Minot Lecture), New England J. Med. 247: 585, 1952.
2. Sturgis, C. C.: Some Aspects of the Leukemia Problem, J. A. M. A. 150: 1551 (Dec. 20) 1952.

improve results, it is essential that the effect of the infection on the heart valves and the reaction of the valves to the injury be understood.

COURSE

It is now widely accepted that the primary insult to the endocardium in all forms of endocarditis, whether bacterial or nonbacterial, is the formation of a thrombus consisting of platelets and fibrin. These thrombi are located along the main line of closure of the valves, oftenest the mitral and aortic and least often the tricuspid and pulmonary valves. The disposition of these thrombi depends on the nature of the injury. If the thrombi are free of bacteria or if they contain bacteria that are promptly killed then organization proceeds, healing takes place, and a scar remains. There may be no valvular insufficiency, or the scar that persists may lead to either valvular insufficiency or obstruction. If there are bacteria in the thrombi and if they are not killed promptly, they grow rapidly and, in many instances, infect the blood. These infected thrombi or vegetations are larger than the nonbacterial forms. They are soft and crumble easily. As a result of the growth of bacteria and their spread to surrounding areas, the thrombi may become massive and may occlude the valvular orifice, or there may be rapid destruction of the valve leaflets with insufficiency; the emboli may be swept into the circulation. From the line of closure, the vegetations grow to the edge of the valve, down into the sinus of Valsalva, along the chordae tendineae, or along the auricular wall, or they extend from the base of the valve into the myocardium to produce a burrowing abscess or perforation of the septum. Thus, this infection that begins as a valvular thrombosis may cause obstruction or destruction of valves with changing heart murmurs and hemodynamics or rupture of chordae tendineae, with the changing heart sounds and murmurs and attacks of pulmonary edema. There may be formation of mycotic aneurysms of the valves or of the sinus of Valsalva, with occasional rupture or leakage into the pericardium and formation of pericarditis; perforation of the septum, with the clinical signs of heart block; an abscess of the heart wall, with rupture; an occlusion of the coronary artery by a thrombus; or, finally multiple emboli to various organs. Thus, the course of this infection may be followed if some of the ways in which the infection behaves are understood.

In the cases of so-called subacute bacterial endocarditis caused by Str. viridans, the vegetations are pinkish, greenish, or yellowish. They rarely cause ulceration and massive destruction of the valves, and the thrombi, or vegetations, are smaller than those commonly seen when the infecting organism is Staphylococcus aureus, pneumococcus, or gonococcus. Auricular vegetations and others involving the chordae tendineae are common, and bacterial emboli are scattered in great numbers to the various organs including the brain, the kidney, and the small blood vessels.

The blood is infected with these bacteria in a majority of the cases, but there may be a bacteria-free stage in which the vegetations show signs of healing or in which they heal completely leaving a scarred, thickened, shortened valve that is draped with large calcified masses.

CHARACTER OF THE THROMBI

The thrombi have been described many times, but Moore [3] examined the vegetations from the heart valves of persons dying from subacute bacterial endocarditis who have not been treated with penicillin. He compared his findings with those from persons who were treated unsuccessfully with penicillin. In short, a vegetation consists of three layers: a central necrotic core of relatively acellular, fibrillar debris and two layers of bacterial colonies surrounding this central core, both of these layers are covered by a delicate fibrillary, acellular material resembling fibrin and platelets. It is apparently difficult for leukocytes to penetrate the barrier of fibrin and platelets. There is also some indirect evidence that anti-infective agents have difficulty in diffusing through this wall.

If the patient lives long enough, there are signs of healing of these vegetations. Healing is characterized by calcification of the vegetations and organization and distortion of the valve. According to Moore, the healing of a thrombus is characterized by fibrosis, hyalinization and calcification of the central necrotic mass, and covering of the surface with endothelium. The effect of penicillin is to reduce or kill the total number of bacteria and to promote the healing of vegetations, since the patients who receive penicillin but who die show more advanced healing than those who are not treated.

The factors that need more study and better understanding are those that promote healing. There are many cases on record in which healing was not completed for many months after the cessation of treatment. There are many reports on "clinically" cured patients who died from other causes but from whom, at necropsy, live organisms were cultured from the heart valves. It has been stated by Cates and Christie [4] that, after death, organisms may be cultured from 30% of the patients in whom the usual clinical criteria for the control of infection were established. Unfortunately, there are no absolute methods of determining that healing has taken place other than through careful study and follow-up of patients.

RESISTANCE TO CHEMOTHERAPY

It is plain that one problem is learning more about the factors that protect the organisms in the vegetations from the full impact of chemotherapy. Attempts have been made to gather and to accumulate more information about the problem of the penicillin penetration of the fibrin barrier in the vegetations so that all organisms are killed. It is well known that micro-organisms can grow in fibrin, and it is well established that penicillin can diffuse into fibrin clots. Also, it has been demonstrated experimentally in animals and in the test tube that micro-organisms growing in fibrin clots can be killed if the concentration of penicillin is adequate. These problems have been studied with great thoroughness by Weinstein and his associates.[5]

3. Moore, R. A.: Cellular Mechanism of Recovery After Treatment, with Penicillin: Subacute Bacterial Endocarditis, Tr. & Stud. Coll. of Physicians, Philadelphia **14**: 55, 1946.

4. Cates, J. E., and Christie, R. V.: Subacute Bacterial Endocarditis: Review of 442 Patients Treated in 14 Centres Appointed by Penicillin Trials Committee of National Research Council, Quart. J. Med. **20**: 93, 1951.

5. Weinstein, L.; Daikos, Y., and Perrin, J. S.: Studies on the Relationship of Tissue Fluid and Blood Levels of Penicillin, J. Lab. & Clin. Med. **38**: 712, 1951. Personal and unpublished observations.

Weinstein and associates found that penicillin diffuses into fibrin clots slowly so that at least two hours are required for the concentration of penicillin in the clot to reach the same concentration as in the surrounding fluid. When a fibrin clot is implanted subcutaneously and the animal is treated intramuscularly with penicillin, the antibiotic diffuses into the clot and persists there for a longer period than in the surrounding tissue fluids. There is also a direct relationship between the quantity of penicillin administered intramuscularly and the quantity of penicillin in the fibrin clots.

If fibrin clots are infected with various organisms (pneumococcus, hemolytic Streptococcus, and Staph. and Str. viridans) all of the same order of in vitro sensitivity and then planted subcutaneously and the animal treated with a single injection of penicillin, it has been shown that Str. viridans behaves differently from the other three organisms. It was found that sensitive pneumococci and staphylococci were eliminated within 8 hours, that hemolytic streptococci were destroyed within 48 hours, but that Str. viridans decreased over a period of 12 hours and then continued to grow out. These experiments suggest that even penicillin sensitive strains of Str. viridans can survive in fibrin clots after exposure to concentrations of penicillin capable of destroying other organisms. These experiments assist the understanding of some of the features seen in patients; that is, intermittent or discontinuance therapy may be effective if the plasma concentrations of penicillin are high enough to penetrate the fibrin barrier and if the concentration of penicillin is maintained in the area for a sufficient period of time to provide maximum killing. They do not explain the reason it is more difficult to kill sensitive Str. viridans in a fibrin clot than other equally sensitive organisms.

These then are some of the problems in planning treatment. It is plain that the main goals of treatment are to destroy all of the micro-organisms in the vegetations and to prevent a recurrence of infection. To achieve these objectives, it is desirable to know how sensitive the infecting organism is to a bactericidal agent and to use these agents in sufficient quantity and for a sufficient period of time to penetrate the fibrin barrier and to kill all of the organisms.

USE OF ANTIBIOTICS

It has been shown that at least 90% of all strains of Str. viridans are inhibited by concentrations of penicillin of 0.01 to 1 unit per milliliter and that the treatment of these strains is usually successful when adequate penicillin is given. If the organism is resistant to one or more units of penicillin then the results of treatment with penicillin alone are not wholly satisfactory. Cases in which this occurs frequently require combined antibiotic therapy or penicillin and renal tubular blocking agents such as probenecid (Benemid).

Selection of Antibiotics.—It is generally agreed that penicillin is the antibiotic of choice for the treatment of all sensitive strains of nonhemolytic streptococci and Str. viridans and that penicillin and streptomycin should be used in combination in all cases of enterococcic endocarditis.[6]

Occasionally, other combinations of antibiotics, such as penicillin and chloramphenicol or penicillin and bacitracin, are useful in the treatment of resistant infections.[7] These resistant organisms can be tested for their sensitivity in vitro in order to obtain a guide for selection of combined therapy.

Forms.—The two most widely used forms of penicillin for the treatment of subacute bacterial endocarditis are aqueous crystalline potassium penicillin G and procaine penicillin G. The first form may be combined with probenecid if high plasma concentrations are desirable and necessary. Procaine penicillin G has been used with success when fewer daily injections are needed.

Dosage Schedules.—Many different dosage schedules have been recommended, and, in spite of the variation of plan, two points stand out. First, the total duration of treatment is as important as the total daily dose of antibiotic. It has been suggested on the basis of study of many patients that the minimum daily dose of penicillin should be at least 2 million units and that treatment should be continued for a minimum period of four to six weeks. Naturally, the daily dosage must be gaged by the patient's response to treatment. There has been a trend recently to use larger doses of penicillin (10 million units) combined with streptomycin (1 to 28 mg.) daily for two weeks or large doses of penicillin alone for only two weeks.[8] Favorable results have been reported. When short-term treatment is employed, the patients should be watched very carefully for signs of relapse or recurrence of infection, since bacteriological relapse often occurs before clinical relapse. Relapses are most frequent during the first four weeks after treatment is discontinued. The final decision concerning dosage must rest with the clinical course of the patient, and new experience with experimental dosage schedules continues to demand attention.

SUMMARY

The over-all results of present treatment can be summed up as follows. 1. Some patients recover from the infection and remain well and asymptomatic for a period of years. This group makes up 60 to 70% of cases. 2. Some recover from the signs of infection and die later of heart failure, uremia, or cerebral embolism. This group accounts for a steady death rate, after the first six months, possibly equal to the normal death rate in patients with valvular heart disease. 3. Patients die during treatment, usually within the first two months, with signs of active infection, heart failure, cerebral embolism, or hemorrhage. This group comprises about 10 to 30% of all cases. 4. Some patients recover from an initial infection only to have reinfection occur at a later date. This group is very small, about 2%.

CONCLUSIONS

We have come a long way on the path to victory or in the war against bacterial endocarditis, but now is the time to consolidate our gains, to assess the present posi-

6. Hunter, T. H.: The Treatment of Subacute Bacterial Endocarditis with Antibiotics, Am. J. Med. **1**: 83, 1946; Use of Streptomycin in Treatment of Bacterial Endocarditis, ibid. **2**: 436, 1947. Cates, J. E.; Christie, R. V., and Garrod, L. P.: Penicillin-Resistant Subacute Bacterial Endocarditis Treated By a Combination of Penicillin and Streptomycin, Brit. Med. J. **1**: 653, 1951.

7. Ahern, J. J., and Kirby, W. M. M.: Cure of Subacute Bacterial Endocarditis with Penicillin and Chloramphenicol: Report of a Treatment Resistant Case, J. A. M. A. **150**: 33 (Sept. 6) 1952.

8. Hamburger, M., and Stern, L.: Streptococcus Viridans Subacute Bacterial Endocarditis: Two Week Treatment Schedule with Penicillin, J. A. M. A. **149**: 542 (June 7) 1952.

tion, and to plan for the future, because there is still much to be accomplished.

What have we gained? We have prolonged the life expectancy of patients with rheumatic heart disease and with congenital heart disease in whom subacute bacterial endocarditis has developed. Moreover, many who have recovered have remained well and are able to be active at least over a period of years. To assure complete victory, we must achieve, first, the prevention of rheumatic heart disease, the complete prevention of hemolytic Streptococcus infection. Next, we must prevent congenital heart disease. This is a task for geneticists and teratologists that needs the attention of all university medical scientists. Third, we must prevent infection, especially oral sepsis and other local infections that commonly invade the circulation and localize on the heart valves when the local defense mechanism is ruptured or penetrated. This objective may be reached by further study of problems of infection.

I believe that these goals can be reached only through the pursuit and accumulation of scientific knowledge through the ideals of experimental medicine and therapeutics, namely, the advancement and transmission of knowledge. Through experimental medicine and therapeutics, advances will continue on a broad front. The example set by Dr. Minot is one that is fully recognized.

65 E. Newton St. (18).

RESULTS OF INTENSIVE (NARCOSIS) AND STANDARD MEDICAL TREATMENT OF EPILEPSY

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The years 1935 to 1939 at the neurological unit of the Boston City Hospital witnessed the beginning of a revolution in the understanding and control of epilepsy. In this clinic, then under the supervision of one of us (T. J. P.), electroencephalography for the first time became a routine clinical service, and its special value in the field of convulsive disorders was demonstrated.[1] The resultant knowledge was utilized to study the effects of various drugs and physiological states on cerebral dysrhythmia.[2] Against this background, one of us (T. J. P.) formulated the conception of a series of specific anticonvulsant drugs, suggested a molecular configuration that has since proved highly successful in several variations, and set up a simple, reliable method of testing the effects of such drugs in animals.[3] The significance of these suggestions and of the theoretical considerations and administrative manipulations that later led to the demonstration of the usefulness of glutamic acid in cases of petit mal [4] and related disorders [5] lies in the fact that they grew out of fundamental neurophysiological considerations and experience. This is a little different from the routine study of chemical series by pharmacologists utilizing established methods of testing,[6] or the routine clinical testing of the products of such investigations,[7] valuable as both may be.

Clinical trial of the new series of drugs was left largely in the hands of Dr. Merritt,[8] who was in charge of the epilepsy clinic in the outpatient department. He meticulously weighed the results and has since continued his interest in similar investigations.[7m] At that time, the foundation of the standard treatment was laid, namely, the principle of starting treatment in new patients with well-known drugs, increasing the dose to the tolerance level, and then gradually shifting to other drugs, which eventually are given in maximal tolerated doses, if relief is not obtained earlier.[7d] Similar studies have been carried out by other members of the original team, now scattered, and their colleagues, with signal success.[9] The recently developed method of rapid determination of optimum medication [10] is clearly an outgrowth of this former association.

The term "standard treatment" apparently was first used by Price and Otto,[7l] without definition. We take it to mean a flexible scheme of treatment in which changes from one drug to another are made until the most effective drug or combination of drugs is found and in which other effective modes of treatment are used, simultaneously or in series, when needed. The chief practical problem is no longer that of attempting to show that anticonvulsant drugs need not be sedatives. This has been done, and the preparation of new variants must be left chiefly in the hands of chemists and pharmacologists. The clinical problems now consist of making a selection among the various drugs and other methods available and searching for new techniques of their application. Methods of selection have been considered in a recent paper [10b]; this paper deals chiefly with methods of use and results.

Although the principles of the standard treatment so far have never been clearly delineated, they have been followed with varying faithfulness in various clinics [11] and, perhaps as a result, with varying degrees of success, as may be seen in the table. (The grading used in the table is that used by Penfield and Steelman.[12]) A few patients in whom the more vigorous and flexible medical treatments failed (grades 0 or 1 response) are suitable candidates for various surgical procedures (chiefly excision of scars or other abnormalities [13]). The remaining unrelieved patients are often dismissed as being untreatable and may have to be institutionalized. It was in the hope of salvaging some of these latter patients that the intensive, or narcosis, treatment was conceived and

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first used. Before describing the method and its results, we should like to record the rules governing use of the standard medical treatment and our results with it, to demonstrate that we have not resorted to a drastic, possibly dangerous, new procedure lightly or inadvisedly.

STANDARD MEDICAL TREATMENT

The following principles of selection of drugs and general conduct of treatment, which we have followed as rigidly and thoroughly as possible for all patients coming into our care, are condensed from a recent paper [10b]:

1. Relatively well-known and nontoxic drugs are preferred to dangerous or untried ones. From the standpoint of serious, permanent toxic effects, diphenylhydantoin (Phenytoin, Dilantin) is probably the safest drug, with phenobarbital and bromides in close competition. Glutamic acid appears entirely safe, but may cause gastric irritation, is often disagreeable or even intolerable to the patient, and is of value in only a small proportion of cases. A significantly high proportion of alarming or fatal reactions have been reported from the use of Mesantoin (3-methyl-5,5-phenylethyl hydantoin), trimethadione, paramethadione, phethenylate (Thiantoin), and phenacemide, the risk increasing about in the order the drugs are listed. Close laboratory and clinical supervision is essential when these latter drugs or bromides are used, and, as Abbott and Schwab [15] have pointed out, this materially increases the patient's economic burden.

2. Treatment should always be started with the most familiar, well-tested, and reliable drug, and newer, less well-known drugs should be added or substituted only for clear cause. Formerly, phenobarbital was the accepted standard,[7d] but the steady success and now obviously low toxicity of diphenylhydantoin has caused us to consider it as first choice, regardless of the clinical type of seizure. The initial dose is usually 0.2 gm. daily and it is gradually increased at the rate of 0.1 gm. weekly. Diphenylhydantoin in oil should be used when gastric irritation results from the use of the sodium salt. It is also useful for infants, for whom the drug has to be mixed with food. Diphenylhydantoin is sometimes effective even when its use produces no effect on the electroencephalogram during a rapid determination. Phenobarbital is our standard second choice. In many of our patients, new drugs undergoing clinical trial have been used after the commercially available ones have proved ineffective. So far, little has been accomplished with such drugs.

3. The dose of each new medicament should be increased gradually until symptoms of overdosage are produced, and then it should be reduced slightly. From our experience, it is wholly clear with respect to diphenylhydantoin and reasonably clear with respect to other drugs used that individual needs and tolerances vary widely and cannot be predicted. In many, perhaps in most, patients the effective dose is close to the toxic dose.

Hypertrophy of the gums, which occasionally occurs as a toxic effect of diphenylhydantoin therapy, can almost always be controlled by vigorous massage.[16] The administration of ascorbic acid may also be tried. Amphetamine is often useful in combating drowsiness caused chiefly by phenobarbital. Toxic rashes and leukopenia in two patients in this series apparently have been controlled by the use of cortisone. Unless a medicament under trial is clearly toxic or useless, its use should be continued until the next drug to be evaluated is being given in reasonable doses.

5. The method of increasing the dose of each drug gradually to the tolerance level, adding new ones to the regimen if the ones previously used are inadequate, and gradually discarding those obviously ineffective or deleterious should be continued until the seizures are controlled or until use of all the available drugs has been tried. About three months are required for thorough trial of each new drug or combination of drugs. This period of experimentation, which is often tedious and sometimes almost intolerable, may often be shortened by use of the method of rapid determination of optimum medication,[10b] which has obvious disadvantages also.

6. The use of phenobarbital and probably, also, of Mesantoin, usually should be avoided if spike and dome or "psychomotor" complexes are present in the electroencephalogram or if definite, typical petit mal, dullness, or psychomotor manifestations are present. Phenobarbital, especially, sometimes seems to convert typical petit mal attacks into psychomotor outbursts, suppressing also the "spike" in the electroencephalogram. The use of trimethadione, paramethadione, or glutamic acid should be avoided except in cases in which some or all of these manifestations are present. Use of one of these latter drugs usually should be accompanied by a maximal tolerance dose of one of the hydantoins (diphenylhydantoin or Mesantoin).

7. Diphenylhydantoin, when the dosage is pushed to the tolerance level, is the drug of choice in patients in whom psychomotor phenomena or periodic dullness [10b] are predominant. Glutamic acid, trimethadione, paramethadione, and phenacemide are preferred next, in that order. Amphetamine may be tried. Vigorous exercise should be required of the patient.

8. Patients should be instructed to report the occurrence of one or a few seizures, and the dose of the drug they are using ordinarily should then be increased, or a new agent should be added. In the long run, especially in growing children, some drug tolerance may gradually develop, and the tolerance dose should be readjusted every year or when symptoms recur.

9. The use of adjuvant therapy, such as exercise, avoidance of strain and fatigue and deleterious activities, and simple psychotherapy, is almost always advisable. Extreme moderation in the use of alcohol must be insisted on.

10. Surgical measures should be considered only when adequate standard medical treatment, as defined, and, perhaps, a trial of intensive treatment, as described in this paper, have failed.[12] Similar medical measures usually have to be carried out after cortical extirpation [17] and only sometimes are more effective afterward than they were before.

These rules are easily followed initially, but the program is often difficult to carry through. Often the first drug tried, usually diphenylhydantoin, is successful at once or as soon as the maximal tolerance dose has been found. In about 26% of our 75 patients, however, the period of trial and error became so prolonged and costly

to the patient that a rapid determination of optimum medication was undertaken and led to its establishment immediately or shortly in 6 patients.

Comparison of Results from Various Methods of Treatment for Epilepsy

Ambulatory Treatment	No. of Patients	Grade of Improvement, %* 4 (seizure-free)	3	2	1	0	Severe, Toxic, or Fatal Reaction to Treatment, %
No specific treatment							
Trousseau [18]	150	13	..	..	..	..	..
Herpin [19]	58	50	..	..	..	..	..
Bromides							
Turner [18]	366	24	..	28	..	..	..
Pollock [20]	85	72	..	..	..	..	..
Arieff [71]	14†	73	..	..	..	..	..
Ketogenic diet							
Wilkins [25]	30	27	..	..	..	..	..
Keith [7f]	190	35	..	18.4	..	46.3	..
Peterman [7j]	123†	..	80	..	..	20	..
Phenobarbital							
Lennox [26]	766	..	65	..	..	..	..
Arieff [71]	48†	90	..	..	..	..	..
Ives [11b]	111†	27	..	..	..	..	..
Diphenylhydantoin							
Merritt & Putnam [7e]	118	58	27	5	..	10	..
Yahr and others [7m]	50†	15	..	9	..	..	..
Boller [6e]	520†	23	..	24	..	15	..
Ives [11b]	92†	20	28	..	..	20	..
Mesantoin							
Kozol [7g]	115†	..	60	..	..	40	..
Lennox [7h]	30†	..	20	..	..	..	..
Loscalzo [27]	67†	32	50	..	..	18	..
Ives [11b]	41†	39	12	..	..	20	..
Glutamic Acid ‡							
Price and others [4]	8†	12	38	25	..	25	..
Zimmerman and others [5b]	7†	70	15	15	..	..	..
Trimethadione ‡							
Lennox [7e]	145†	33	30	21	..	16	..
Ives [11b]	44†	7	23	..	..	32	..
Phethenylate							
Peterman [7j]	57†	..	65	..	..	31	..
Phenacemide							
Tyler and King [28]	1,562†	37	..	31	..	32	21
Davidson and Lennox [29]	178†	3	19	24	..	..	15
Standard treatment							
Ives [11b]	212	31	..	..	..	..	..
Yahr and others [7m]	319	48	..	37	..	..	..
Present series (without intensive treatment)	75	56	4	7	33	..	..
Radical Treatment							
Excision of cortical scars							
Penfield [12]	59†	25	30	14	12	18	1.3
Excision of motor cortex							
Pilcher and others [14]	41†	20	30	21	..	..	4
Intensive medical treatment							
Present series	25	64	20	16	..	..	0
Standard and/or intensive treatment							
Present series	75	77	11	12	..	..	0

* Percentages are rounded to nearest digit.
† Selected patients; the basis of selection was not always clear.
‡ Effect on petit mal or psychomotor attacks.

RESULTS OF STANDARD TREATMENT

The patients used for evaluation of the strict standard treatment were unselected, except that the majority had been unsuccessfully treated elsewhere. They consisted of 33 patients seen in the outpatient clinic of the Cedars of Lebanon Hospital and 52 seen in private practice over a five year period (1947 to 1951, inclusive). Although relatively few children are included in this series, on the whole, treatment has been more successful among the children than among the adults. Patients in whom treatment was prematurely stopped for reasons unrelated to the disease, those treated for less than one year, and those in whom the seizures were obviously due to some gross lesion requiring surgical treatment were excluded. Otherwise, no special attempt was made to classify the patients into cryptogenic and symptomatic groups, because in our experience, as in that of Yahr and co-workers,[7m] such attempts at classification do not seem greatly to affect therapeutic results. Owing to the length of time required to complete the many steps of the standard treatment in difficult cases, a large group remains in whom treatment is not yet finished. The proportion of such incompletely treated patients is especially high in the clinic.

The results obtained with the method described are recorded in the table, where they are compared with other series reported in the literature and with the recovery rate in untreated series of patients. Trousseau gives this latter rate as 13% [18] and Herpin as high as 50%.[19] It probably is significant that prior to the advent of diphenylhydantoin, statistics showing the proportion of patients maintained seizure-free are extremely rare.

As many authors have noted, conscientious evaluation of results is difficult to attain. We have adopted the simple classification reported by Penfield and Steelman,[12] into which most reports may be fitted with reasonable accuracy. These authors group results as follows: grade 0, failure; grade 1, 25% improvement; grade 2, 50% improvement; grade 3, 75% improvement; and grade 4, 100% improvement. This rating is designed for a study of the results of surgical treatment, which was considered concluded at the time the patient left the hospital. The designation of such a definite end-point is not possible in assessing the results of medical treatment, including the intensive form, the full results of which may not be apparent until weeks or months after the period of narcosis has ended. We have, therefore, perhaps arbitrarily, taken the position that the standard treatment is completed only after the patient is either relieved of his seizures for a year or has been given a thorough trial of all or almost all forms of medication likely to help him. In some cases, this trial periods was accelerated by the use of the method of rapid determination,[10b] and certain reasonably obvious omissions were made; for example, patients who had grand mal alone were seldom given a trial course of trimethadione, paramethadione, or glutamic acid. It has been our policy to postpone the use of the drastic and expensive intensive treatment until the full course of the standard treatment has been given.

The criticism may be made, with some justification, that this group of "completely treated" patients contains an unduly large proportion of patients likely to be relieved by almost any reasonable form of treatment. It is true that control of the seizures is the commonest reason for transferring a patient out of the "incompletely

treated" category. During the five year period in which most of this data was being collected and 75 patients had been established on a level of medication we considered optimum, with or without the intensive treatment in patients not seizure-free, we had also begun treatment of 25 others, which we do not yet consider completed, since the use of several drugs remains to be tried in each. Seventeen (68%) of these latter patients have now attained grade 3 improvement, that is, they are free of grand mal seizures or are able to work.

Of the 75 patients in our "completed" series, 58 are taking diphenylhydantoin in doses up to 0.6 gm. daily, 12 are taking phenobarbital, 12 Mesantoin, 7 trimethadione, 3 paramethadione, 2 each phethenylate, glutamic acid, and AC 268 (5-isopropoxymethyl, 5-phenyl hydantoin [Parke-Davis]) and 1 each phenacemide, Hibicon (3-chloro-N-benzylpropionamide), and mephobarbital (Mebaral). The various combinations of these drugs empirically derived are too complicated to report. Milontin (N-methyl-α-phenylsuccinimide), Nuvarone (3-methyl-5-phenylhydantoin), and several other drugs still in the experimental stage of use have been given trials but have not seemed as valuable as those just listed.

Ives,[11b] Peterman,[7j] and others refer to phenobarbital as the least toxic anticonvulsant drug available. We have been unable to corroborate this in our series. In our experience, phenobarbital is always toxic in doses over about 0.1 gm., producing a drowsiness or depression that seriously impairs the patient's work ability and social adjustment. Further, deaths from the suicidal use of phenobarbital [20] far outnumber deaths questionably attributable to the use of diphenylhydantoin.

INTENSIVE (NARCOSIS) TREATMENT

Since a certain proportion of failures occurs with every type of treatment of epilepsy, no matter how intensive or flexible it may be, the search for better forms of treatment must continue. The idea that some relatively brief, intensive medical treatment may be found has many roots, stretching far back into the past.

It has long been known that surgical procedures of many types may be followed by long periods of relief from seizures. The series of 62 cases of craniotomy, with 42 "cures," collected by Billings [21] well exemplifies this. Many physicians can remember when it was considered good for epileptics "to have their colons reduced to semicolons," as Dr. Frederick Collins expressed it, and the statistical results as reported were encouraging. Relatively brief periods of starvation or longer periods of ketosis are sometimes effective in bringing about a remission of seizures, but either procedure is disagreeable to the waking patient. Possibly, a short period of ketosis may be combined with a prolonged period of narcosis, simulating anesthesia. One of us (T. J. P.) used phenobarbital for this purpose in a few patients about 10 years ago, but without much success. According to Lennox,[22] this same idea was put into practice by Cooter more recently. One-third of his patients are reported to have remained seizure-free after 10 days of such treatment, but it was abandoned after several serious mishaps. A case reported in 1942 seemed significant in several respects: "An interesting case was described by Dr. E. S. Montgomery of Tarentum, Pennsylvania, who wrote in February, 1942, of a patient with pneumonia who was given at each time of sulfapyridine medication a capsule of dilantin [diphenylhydantoin] sodium making a total of 3.2 gm. in fifty hours at which time the patient became comatose with a pulse rate of 42 per minute. The pupils were unequally dilated, the tongue and buccal membranes were dry, the blood pressure 60/20-mm. Hg and there were no tendon reflexes. Fifty hours after the overdosage was discovered the patient asked for water and recovery from this point was uneventful." [23] Dr. Montgomery writes us that this patient is still in good health and free of seizures, and he adds, "I have treated 9 additional cases with large doses of dilantin sodium and 7 of these patients have been symptom free for periods beyond six years. Some of the 9 patients were given doses of dilantin in excess of 4.0 gm. daily for varying periods of 3 to 10 days."

Because of these experiences, we decided to determine the effect of prolonged narcosis, produced chiefly by diphenylhydantoin, combined with the production of ketosis, administration of glutamic acid, and frequent inhalations of carbon dioxide, which are known to abolish slow wave activity in most patients.[2b] The following case reports illustrate the nature of some of the problems that led us to feel justified in taking such a drastic step.

REPORT OF CASES

CASE 1.—A 33-year-old man, referred to us by Dr. Daniel Castile of Riverside, Calif., had sustained a skull fracture and cerebral concussion 11 years prior to his first visit July 28, 1947. At age 26 grand mal and minor seizures had developed. The grand mal seizures were often preceded by an aura of numbness and tingling of the left hand. They occurred one to five times per week without medication; however, when the patient received maximum doses of diphenylhydantoin, they occurred one to two times a month. In 1946, the patient had bilateral burr holes placed for removal of a subdural hematoma that occurred after a head injury sustained during a grand mal seizure. In the previous three years, the patient had had difficulty with his gait.

Neurological examination revealed the following positive findings: Bilateral burr holes were palpable in the frontoparietal and temporal areas. There was mild left lower facial paresis, and mild bilateral vertical nystagmus. The temporal margin of the left optic disc was indistinct, and the temporal half of the disc was bluish-white, especially in the superior temporal quadrant. The reflexes were hyperactive throughout, and Babinski and Hoffmann signs were elicited bilaterally. The abdominal reflexes were absent, but the cremasteric reflexes were intact. The patient had an unsteady, broad-based gait and a slightly positive Romberg sign. Dr. N. A. Bercel's interpretation of electroencephalograms was as follows: "A marked dysrhythmic record at 100 μv maximum. Both frontomotor areas are more involved than the rest of the cortex. There is only a faint suggestion that the left one is the more active side." Other routine laboratory examinations showed nothing of apparent importance.

The patient had been given many different drugs in large doses, including bromides, phenobarbital, and diphenylhydantoin. After some experimentation, it appeared that the following combination of drugs was most effective for him: diphenylhydantoin 0.3 gm., mephobarbital 0.3 gm., Mesantoin 0.4 gm., and trimethadione 1 gm. daily. These amounts represented approximate subtoxic doses of each. The patient felt slightly unsteady but had an average of only one attack daily.

Since the patient was still incapacitated, he was admitted to the Cedars of Lebanon Hospital Dec. 3, 1947, for further study. A ventriculogram was made to make certain that no

hematoma or gross scar was present. This showed five old trephine openings, as expected, and a moderate symmetrical dilation of the ventricles. Electroencephalograms were made and showed dysrhythmia, with abnormalities in the anterior third of both hemispheres. Inhalation of a carbon dioxide mixture promptly temporarily wiped out the abnormalities.

As no other means of treatment seemed available intensive treatment was considered. Its theoretical background was explained to the patient and his relatives, and the procedure was accepted by them. Beginning Dec. 5, 1947, the patient was given 0.9 gm. of diphenylhydantoin by mouth daily, with phenobarbital as needed to keep him drowsy, and inhalations of 5% carbon dioxide with 95% oxygen for five minutes every two hours. Special nurses were in attendance day and night. The patient was kept so drowsy that he lay quietly and did not talk but would sometimes arouse between doses and take nourishment and fluids or attend to bodily functions. After the second day, intravenous injections of glucose were required to prevent dehydration. The anticonvulsant medication was withdrawn Dec. 8, and the patient became sufficiently alert the following day to attend to his own needs, so the special nurses were dismissed. On Dec. 10, he was given two doses of 15 mg. of amphetamine to overcome drowsiness and was permitted to return home. Prescribed medication for home use consisted of diphenylhydantoin 0.3 gm., mephobarbital 0.3 gm., Mesantoin 0.4 gm., and trimethadione 1 gm. daily, which was the same amount the patient had taken before his operation.

The patient had no more seizures and returned to his occupation as a rancher. This period of improvement lasted 10 months, when he again began to have minor seizures, which he attributed to a severe emotional disappointment. By this time, we had had more experience with the intensive treatment, and we recommended that it be repeated in a more drastic form. Accordingly, on Sept. 22, 1948, similar precautions being taken, the patient was again given 0.9 gm. of diphenylhydantoin daily, supplemented by 0.2 gm. of phenobarbital every two hours or as needed to keep him drowsy, and a carbon dioxide-oxygen mixture as before. He became deeply narcotized by Sept. 24, when evidences of mild bronchopneumonia accompanied by a diffuse erythema developed. Diphenylhydantoin and phenobarbital administration was, therefore, discontinued. The patient continued to sleep deeply, still receiving inhalations of the carbon dioxide-oxygen mixture. His respiration became shallow, and the periods of administration of carbon dioxide were lengthened. A slight fever and rales in both sides of the chest developed. Antibiotics were given. The patient had several mild seizures daily from Oct. 6 to 12. He was, therefore, given the maintenance medication he had been taking on admission. Because the seizures continued, on Oct. 14 narcosis was induced again with the same combination of drugs previously given. This was continued through Oct. 19, this time without complication. The patient was awake and able to take care of himself on Oct. 23 and was discharged Oct. 26, after which he began taking the same medicaments in the same dosage that he had been taking on admission, plus 1 gm. of phenacemide daily. He has been followed closely since that time and has had no major seizures. Occasionally he had tingling of the fingers of the left hand when dropping off to sleep, but even this has disappeared in the last year. The left arm has grown weaker and more spastic, however. The phenacemide was omitted from his list of medicaments in 1949, and the dose of Mesantoin was decreased in 1951. He has been working steadily and has been granted a driver's license.

CASE 2.—A boy was first referred to us by Dr. Norman Reider of San Francisco July 27, 1949, when he was 17 years old. He had had his first attack at age 12. He would walk around in a circle and then fall unconscious to the floor. The frequency of these attacks gradually increased, until they occurred about once weekly. In the later attacks, the patient's facial muscles would twitch, and he would turn his head to one side or the other. In some attacks, he bruised or burned himself. Within a year before he was referred to us he had begun to be rebellious, surly, and ill-behaved, although highly intelligent.

Pneumoencephalograms had been performed, with negative results. Several electroencephalograms had been made, and all showed generalized, paroxysmal, nonspecific dysrhythmia, with occasional invasion of wave and spike complexes. Results of other examinations had been noncontributory. The patient had received the following medicaments daily at various times from eight different physicians, without relief: diphenylhydantoin 0.4 gm., phenobarbital 0.3 gm., Mesantoin 0.6 gm., mephobarbital 0.3 gm., and glutamic acid 20 gm.; in addition, regulation of the acid-base balance had been tried. Our clinical examination, including roentgenograms of the skull and electroencephalograms contributed no new information. Because most of the steps of the standard treatment method had already been carried out and because the patient had come a long distance for treatment, a period of intensive treatment was decided on.

While under the constant watch of special nurses, beginning July 30, 1949, the patient was given 0.9 gm. of diphenylhydantoin and 15 gm. of glutamic acid daily, with enough phenobarbital (up to 0.2 gm. every 2 hours) to keep him drowsy. Inhalations of a carbon dioxide-oxygen mixture were given every hour. In addition, 300,000 units of procaine penicillin was given intramuscularly twice daily. A ketogenic diet was ordered, but by Aug. 3 the patient was too drowsy to eat or drink and had to receive fluids intravenously. He had to be catheterized, and, finally, tidal drainage of the bladder was instituted. On Aug. 6, diphenylhydantoin and phenobarbital administration was stopped, but the patient did not awaken until Aug. 11.

This period was utilized for rapid determination of optimum medication, a procedure that was at that time in process of development. A comparison of records made it clear that of the three drugs tested, trimethadione in a dose of 2 gm. had the greatest effect on the slow waves, but diphenylhydantoin in a dose of 1 gm. and Mesantoin in a dose of 1 gm. also produced substantial improvement. Phenobarbital produced minimal improvement and phenacemide none.

On awaking from this period of narcosis, the patient rapidly regained normal vigor and alertness. On discharge, diphenylhydantoin 0.5 gm. and trimethadione 0.3 gm. daily was prescribed. From that time, the patient has had no seizures of any kind or periodic dullness. His irritability rapidly disappeared. He was somewhat sensitive to bright lights, and this symptom was overcome by reduction in the dose of trimethadione. The patient has recently married and is attending college.

CASE 3.—A 35-year-old man was first referred to one of us (T. J. P.) by Dr. Wilder Penfield in 1944. Convulsive seizures had developed in this man at the age of 7 years, but with phenobarbital medication he had had a remission at the age of 13, which lasted 4 years. Seizures then recurred, with a prodrome of generalized weakness and nausea as well as hesitation in speech and, occasionally, diarrhea. They occurred at irregular intervals, on an average of four per year. During some seizures, the patient sustained bruises and cuts about the head. He had been given phenobarbital and diphenylhydantoin.

General physical and neurological examinations revealed nothing of apparent significance. Electroencephalograms taken at the Montreal Neurological Institute showed "bisynchronous wave and spike disorder of moderate severity." This examination has since been repeated at intervals, and the results have been uniformly the same. Results of other routine laboratory studies have been noncontributory.

The patient's dose of diphenylhydantoin was systematically increased to the tolerance level (0.4 gm. daily), and regular exercise was prescribed. He improved greatly, and, except for occasional lapses in medication during intercurrent illness, was seizure-free for five years. During this period, he got married, obtained a driver's license, and worked steadily as a broker. In 1947, he began to have auras of seizures, and Mesantoin, 0.1 gm. daily, was added to his drug regimen. Further increases in medication resulted in ataxia. During 1948 and 1949, the patient had four seizures and finally lost his job. In May, 1949, his wife filed suit for divorce, and he went into a severe depression and had to be institutionalized. He came to Los Angeles in July, 1949, for a reconsideration of treatment, but the seizures continued even when he was

taking subtoxic doses of his medicine. Finally, the intensive treatment was suggested to him and was begun Aug. 19, 1949.

While under the constant supervision of special nurses, the patient was given 0.9 gm. of diphenylhydantoin and 15 gm. of glutamic acid daily and enough phenobarbital, up to 0.2 gm. every two hours, to keep him drowsy. He was given inhalations of a carbon dioxide-oxygen mixture for five minutes every hour. A ketogenic diet was prescribed, but by Aug. 22 he was to sleepy to eat or drink. As he did not void spontaneously he had to be catheterized, and finally tidal drainage was instituted. Dihydrostreptomycin, 0.3 gm., and penicillin, 50,000 units, were given every three hours. Intravenous injections of 5% glucose solution were given to prevent dehydration.

On Aug. 24, the administration of phenobarbital was discontinued, and the period of recovery was used for a modified rapid determination of optimum medication as used at that time. This showed clearly that trimethadione had the greatest normalizing effect on the patient's dysrhythmia with phenobarbital next best and Mesantoin third. Diphenylhydantoin and phenacemide showed little effect on the record. Therefore 0.8 gm. of Mesantoin and 0.3 gm. of trimethadione daily was prescribed. Up to the following February, the patient had five seizures, at longer and longer intervals, but has had none since then. Meanwhile, he has completed the necessary work and received the degree of master of arts. On his own initiative, he gradually reduced and finally omitted all of his medication up to February, 1953, when he began taking the drugs again. It seems to us unlikely that this striking improvement can be ascribed to emotional causes, since his life is still filled with disappointments and frustrations.

CASE 4.—An incapacitated business man, 48 years old, was first seen as a private patient July 11, 1950. He had been generally well and had worked hard until 1940, when he began to have seizures, with sudden loss of consciousness, falling, twitching of the extremities, and sometimes foaming at the mouth. They lasted as long as four minutes and occurred at irregular intervals; he never had less than 4 and had as many as 17 a year. Most attacks were preceded by an aura of a sensation of flushing of the face, which often occurred also without definite attacks, sometimes as often as 23 times a day. Within a year of the onset of his symptoms, the patient was seen at a well-known clinic in another city, where a ventriculogram was made and a left-sided exploratory craniotomy was performed. After the craniotomy, he had frequent paresthesias of the right upper extremity, despite the use of various drugs, including phenobarbital, diphenylhydantoin, and Mesantoin. He dates his complete incapacity from that time. He took 0.4 gm. of phenobarbital daily, and this was later changed to 0.4 gm. of diphenylhydantoin.

For financial reasons, he requested transfer to the outpatient clinic of the Cedars of Lebanon Hospital. There a lumbar puncture was performed, with results within normal limits. An electroencephalogram was made and showed a pronounced dysrhythmia, with a slow wave focus over the left hemisphere. The dose of diphenylhydantoin was gradually increased to the tolerance level, 0.5 gm. daily, and this was supplemented by 0.1 gm. of phenobarbital. This controlled the patient's grand mal seizures, but the frequent focal sensory seizures (up to 10 daily) prevented his working. In the hope of bringing about an economic rehabilitation, a rapid determination of optimum medication was advised. This was begun on Oct. 30, 1950. Phenobarbital was found to have the greatest beneficial effect on the electroencephalogram, but Mesantoin, glutamic acid, and paramethadione produced slight improvement.

Since the patient had already had a long clinical trial with phenobarbital and Mesantoin, the next logical step seemed to be to subject him to a period of narcosis treatment. He was hospitalized for this purpose on Nov. 6. Constant special nursing was provided. He was given 0.3 gm. of phenobarbital orally every two hours until asleep, 1.5 gm. of diphenylhydantoin every eight hours, 10 gm. of glutamic acid every eight hours while able to swallow, inhalations of 10% carbon dioxide, 300,000 units of penicillin daily, and fluids intravenously as needed. He was deeply asleep within two days but could still be persuaded to swallow the diphenylhydantoin capsules. After this, no food was given by mouth. On Nov. 11, while he was still asleep, his temperature arose to 104 F. It was found that his urine was infected. A tidal drainage apparatus was installed, and use of all sedatives was discontinued. The temperature was normal within three days, and the patient gradually recovered consciousness. He was discharged from the hospital Dec. 4, and Mesantoin 0.6 gm., glutamic acid 15 gm., and paramethadione 1.8 gm. daily was prescribed.

The patient has been followed in the clinic. In May, 1951, he had one grand mal attack, and he complained of slight discomfort in the old craniotomy scar. That was his last major attack; on July 1, 1952, he reported that he had had no attacks of any kind for 13 months and was working regularly as a bookkeeper.

A synopsis of the entire series of patients treated by the intensive method is given in the table. It will be seen that seizures are controlled in 66% of patients with difficult, recalcitrant seizures, and in only about 15% can the treatment be considered to have failed. The results compare favorably with those from surgical treatment (see the table).

AVOIDANCE OF COMPLICATIONS IN INTENSIVE TREATMENT

While the cardinal points in intensive treatment were utilized from the first case, experience has caused us to modify the details. It was clear at once that patients receiving the treatment should have a nurse in constant attendance, and this is still required. A suction apparatus should be available. The only serious complication of the treatment was pneumonitis, which was seen in three of the early patients. In all of these, a ketogenic diet and glutamic acid was being given by nasal tube. We then learned to allow ketosis due to starvation to develop and to administer fluids intravenously. In future cases, we plan to give glutamic acid intravenously also. As a further precaution against pneumonitis, we give 300,000 units of procaine penicillin intramuscularly daily. We still feel safer in having a skilled anesthetist available on call, in case intratracheal insufflation or aspiration is required.

As time went on, we learned to induce sleep with massive doses of diphenylhydantoin, usually 4 gm. for an adult. If this does not produce a comfortable relaxation, we give paraldehyde [24] orally or rectally or phenobarbital intramuscularly as a supplement. If the patient is in such deep coma that he cannot swallow, subsequent doses of diphenylhydantoin (usually 1.5 to 2 gm. daily during the period of narcosis) are given in suppositories.

Inhalations of 10% carbon dioxide in 90% oxygen are given by mask for 10 minutes every hour. Perhaps this dose should be increased, at least in some cases. We have tried administration of a lower concentration continuously in a tent, but the gas escapes too rapidly. At present, we are experimenting with continuous administration of low concentrations by means of a special mask. Patients are allowed to void spontaneously. Occasionally, catheterization or tidal drainage is necessary. Defecation is managed with enemas.

As a rule, four days has been taken empirically as a satisfactory duration of deep sleep. When the treatment has been interrupted earlier, the results have seemed less good; when the sleep has continued longer, the risk of

complications (pneumonitis and excessive loss of weight) has seemed greater. Usually, all medication is then stopped, and sometimes amphetamine is given to shorten the period of awakening, which is often a difficult one, since the patient may be delirious. If necessary, paraldehyde is given to control excitement. As the patient approaches a normal state, his preoperative medication is begun again and continued indefinitely.

COMMENT

Even in the most successful cases, favorable results may not be seen immediately. Sometimes there is an actual exacerbation of preexisting behavior disorders, which lasted in one case as long as six weeks. Sometimes, also, the patient will have an isolated seizure within three months after the intensive treatment, then will have no more. The results in such cases are considered to be successful.

A long period of freedom from attacks was followed by relapse in three cases. One was that in the patient described in case 1, the first in the series. Since having a second course of treatment, the patient has been seizure-free and working for four years. In another case, a repetition of the treatment moderated but did not control the seizures. In the third, the attacks have remained under control for over a year. Relapse occurred in a fourth patient, who was placed in an institution, where her maintenance medication was discontinued.

There was clear evidence of a gross lesion of the brain in seven patients. In three, craniotomies had been carried out. In others, "spikes" were demonstrated in the temporal region in an electroencephalogram taken during sleep. Such patients may be considered candidates for temporal lobectomy. It has, however, been our feeling that it is more conservative to administer the intensive treatment first. If this is unsuccessful in patients in whom surgical procedures seem indicated, we hope to carry them out. There has seemed to be little difference in results obtained between the cases in which the epilepsy was presumably symptomatic and those in which it was cryptogenic. The worst results were obtained in seven patients who had severe deterioration. Among these cases two complete failures occurred, but there were also three cases in which gratifying successes were obtained.

While no patients in this series have died, there certainly is some potential risk in the treatment. Prolonged narcosis for other purposes has resulted in an appreciable mortality, which might be decreased by the precautions now available (avoidance of gavage, use of suction and carbon dioxide inhalations, and administration of antibiotics). This is necessarily an expensive treatment. A two week stay in the hospital, with continuous special nursing, should be provided for, and this period occasionally is exceeded. The expense might be greatly diminished if the treatment were given in special institutions or sanatoriums rather than in general hospitals and if one or two nurses could take care of a group of patients undergoing treatment simultaneously. Despite these disadvantages, most patients whose seizures are uncontrolled accept the treatment gladly.

SUMMARY

An outline of rules for the conduct of the standard ambulatory treatment of epilepsy, as employed by the authors, is given. In cases in which circumstances have permitted these rules to be followed strictly to their conclusion, as high as 56% of patients have been maintained seizure-free for significant periods. Even among patients in whom the treatment has been only partially carried out but has been continued for more than a year, 68% are free of major seizures and are also able to work or go to school.

In the 25 patients unrelieved by the complete standard treatment as outlined, a new form of intensive, or narcosis, treatment has been administered. This consists of the administration of massive doses (up to 4 gm. daily) of diphenylhydantoin, sometimes combined with paraldehyde or another soporific. Ketosis from starvation is allowed to develop, and the patient is given inhalations of a carbon dioxide-oxygen mixture every hour. Other details of treatment and precautions necessary are described. The period of sleep usually lasts four days and the entire treatment about two weeks. Following such treatment, 64% of patients previously unrelieved by the standard treatment have been maintained seizure-free. In the entire series of 75 patients, attacks were finally controlled in 58 (77%).

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Education for Professional Services.—Since Plato first wrote of the necessity for educating men to wisdom, scholars and thinkers throughout the Western world have repeated his message again and again. . . . But today our educational system is fragmented, stressing occupational values, and in danger of letting our civilization follow the path, like Rome and Athens, to decay and destruction. . . . The modern barbarians do not destroy science and technology, they do not wipe out the machine values but instead convert them into terrible forces of evil and death so that those who would resist their mad rush must out-do them in ruthlessness. What they do destroy with devastating thoroughness is the liberal culture of the people. They destroy their roots into the past, their libraries, their free press, their religion, their belief in the essential dignity of man. In short—destroy the education which makes men free. . . . It seems self evident that one of the elementary functions of primary and secondary education is to inculcate the desire to read and to develop at least the rudiments of taste for the literature of our own tongue. That we fail to accomplish this in any large measure is, I believe, the conviction of most men who teach in college and university and are thus in a position to evaluate the accomplishment of the schools. . . . The bald fact is that we, as a people, no longer hold liberal education in high regard; we do not think very well of the education which nourishes man's spirit. Instead, accepting the pragmatic utilitarianism of our day, we have filled the student's time with whatever seemed to him and to his parents to be most immediately profitable; the vocationalized, the specialized, the elective and the electric, with the transient fads and interests of the day. We have established no standards, acknowledged no immutable values and adhered to no common faith. With amazing arrogance we have turned our backs on the past, thus ignoring Santayana's wise observation that "Those who cannot remember the past are condemned to repeat it." With sublime faith in the belief that in this new age of science and enlightenment man's salvation would be achieved with slide rule and analytic balance, we have piled specialization upon specialization with the inevitable result—fragmentation of education.—S. Dorst, M.D., Education for Professional Services, *The Pharos of Alpha Omega Alpha Honor Medical Society*, May, 1953.

ANESTHESIOLOGIST'S RESPONSIBILITY TO THE PATIENT

CHAIRMAN'S ADDRESS

R. J. Whitacre, M.D., Cleveland

Anesthesiology is on the threshold of its greatest contributions to the safety and mental well-being of the patient. In the past, the initial responsibility of the anesthesiologist was to make the patient comfortable and to provide adequate muscular relaxation and reflex depression during surgery. These two objectives are being accomplished in the vast majority of operations; however, the obligations of the anesthesiologist are now distributed over a wider area. Greater attention must be given to the broader, and perhaps more important, aspects of patient care. Successful surgery defeats its own end if the anesthesia service is deficient. I am confident that in the future greater emphasis will be placed on safety to the patient and that more attention will be devoted to the understanding of the patient's problems. My discussion will be limited to these two points. Measures to decrease the danger of surgery and to increase the satisfaction of the patient are of fundamental importance to his welfare and are essential to the development and progress of anesthesiology.

INFORMATION REQUIRED

During the past 20 years, anesthesiology has progressed through several interesting phases. Opinions have differed widely regarding the importance of anesthesiology and the pattern that should be followed in its application. As in most phases of medical care, time and experience will eventually dictate the proper solution to our problems. The history of medicine has repeatedly shown that if it is possible to devote more attention to the factors of fundamental importance, we will more readily obtain our objective, better care of the patient.

The safety of anesthesia administration requires a particular and intimate consideration, because many of the inherent dangers are not adequately understood. Regrettably, we are handicapped by a deficiency of factual information about complications and deaths that occur during and after anesthesia. While many exhaustive surveys and analytical reports are published annually on a great variety of medical subjects, there is an unfortunate lack of comparable material on the hazards related to anesthesia. Perhaps because the personal experience of each surgeon or anesthesiologist is necessarily limited, the importance of anesthesia as a cause of morbidity and mortality is often underestimated.

During the past decade, several factors have forced us to revise our opinion of the importance of the dangers associated with anesthesia. One factor is the great increase in the number of elective operations on good risk patients. A fatality in this group naturally causes greater public and professional concern. There also has been a definite increase in the number of complex and technically difficult surgical procedures of longer duration. The successful outcome of these operations is more than ever dependent on the quality of the anesthesia administration. The third change is that larger numbers of poor risk patients benefit from the advances in surgical practice. Many of these patients would have been considered inoperable a few years ago. The need of precautionary measures and more painstaking anesthesia care for such patients is obvious. Many of these developments have occurred so swiftly that we have failed to appreciate the necessity for careful evaluation of the effects of anesthesia. A thorough understanding and analysis of these problems are vital if we are to avoid a false sense of security regarding the risk accompanying anesthesia.

The advice of every anesthesiologist is sought at one time or another regarding problems in his field. As consultants, we sometimes mislead those who seek our advice by stating or implying that the use of certain drugs or techniques will eliminate the danger of anesthesia. The impression is often gained that we, the consultants, do not encounter difficulties. The fact is, a discussion within any group of anesthesiologists with substantial clinical experience soon discloses that few anesthesia complications ever find their way into the literature.

Another indication of the reluctance of anesthesiologists and surgeons to present the problems encountered in the operating room has been the difficulty experienced by those who have endeavored to establish anesthesia study commissions. Many years ago, we were impressed with the potential value of the Anesthesia Study Commission established in Philadelphia under the direction of Dr. Henry Ruth. About 14 years ago, when we began an effort to study anesthesia problems systematically on a regional level, the prevailing attitude varied from indifference to active opposition.

The cooperation of clinicians has vastly increased in recent years. More factual information is necessary, however, before we can evaluate the real importance of anesthesia with a reasonable degree of accuracy. The nature of most anesthesia complications is such that great care must be exercised to avoid apprehension or loss of public confidence. Because it is our duty to provide the greatest degree of safety for every patient who enters the operating room, no one should deceive himself about the actual dangers associated with anesthesia.

MORE ANESTHESIOLOGISTS NEEDED

Fortunately, great progress has been made toward realization of the anesthesiologist's foremost ambition, making anesthesia safe. This progress has included the development of new drugs, new techniques, and better understanding of the basic sciences as they relate to anesthesiology. But a factor of equal importance is the

From the Department of Anesthesiology, Huron Road Hospital.
Read before the Section on Anesthesiology at the 102nd Annual Session of the American Medical Association, New York, June 3, 1953.

application of all available knowledge to each patient. This can be accomplished only by a larger number of qualified anesthesiologists. This need is emphasized further by the increased number of operating room problems that cannot be managed effectively unless the anesthesiologist has one or more associates to assist him.

Another sphere with which we are concerned is the obligation inherent in the patient-physician relationship. This includes sympathetic understanding of the patient as well as professional evaluation of his condition and his requirements in relation to adequate preparation for impending surgery. From the patient's point of view, the anesthesiologist's preoperative visits provide the personal consideration that results in greater confidence, understanding, and freedom from fear. While it may not be generally conceded that the patient requires an explanation of the type of anesthesia to be administered, there can be no doubt that a candid response by the physician to intelligent questions will prove beneficial. If the patient is apprehensive about a certain anesthetic, this should be taken into consideration and the prejudice respected if possible. An anxious and unrelaxed state induced by uncertainty is harmful and disturbing. The patient should be enlightened regarding the procedure ahead and the reasons for certain restrictions.

There are many instances in which timely preoperative attention has meant the difference between life and death. Greater safety in the operating room will not be achieved until the anesthesiologist can discharge his obligation toward each patient and his problems. Postoperative visits result in better supervision of the physical needs of the patient. In addition, they foster good will. Preoperative and postoperative visits are a phase of anesthesia service that is of great importance, but its benefits will not be realized by all patients until there are greater numbers of trained anesthesiologists.

Only by increasing our numbers can the obsolete standards of 15 or 20 years ago be discarded. At that time, the hospital staff that included one anesthesiologist was considered adequately staffed. This was a great step forward; however, under that system personalized service was impossible. Today there is no valid reason for every person entering the operating room not receiving expert attention. This responsibility to the patient can only be fulfilled if we attract enough physicians and train them to be competent anesthesiologists.

The number of resident training programs was limited in the past. This made it difficult to provide anesthesia instruction to a sufficient number of physicians. This defect has now been remedied, and, at the present time, there is no shortage of educational facilities. The problem now is to find ways and means of interesting a greater number of physicians in the practice of anesthesiology. I do not mean to infer that there is a decreased interest in anesthesiology. The situation is one in which the demand for qualified anesthesiologists is growing so rapidly that we are unable to keep pace with it.

Perhaps we should consider the successful manner in which so many well-trained surgeons were produced. This was accomplished by making surgery attractive to the young physician. Since this field offered ample professional recognition and incentive, adequate numbers of competent surgeons are now available in virtually every community in the country. If we are to meet our responsibility to the patient by providing a degree of anesthesia service comparable to the progress made in surgery, the obvious approach is to make sure the incentives and opportunities provided by our specialty attract an ever-increasing number of physicians. Any attempt to induce greater numbers of capable men to study anesthesiology is doomed to failure unless it places proper emphasis on professional prestige and community esteem. We know there is sufficient stimulus from a scientific point of view. There are probably those who would maintain that this is the only inducement needed to attract men of high caliber. I do not believe that this premise will effect a satisfactory solution. Recognition and opportunities are powerful incentives to provide outstanding service. When the practical benefits of the study of anesthesiology are more apparent and less controversial, the problem of procuring the right type of applicant will be resolved.

Lay and medical people alike have questioned the relationship between the program of attracting young men and better care of the patient. The critics of the broad policies outlined here have, however, suggested no constructive plan to fill the need for an adequate number of anesthesiologists. The solution demands the thoughtful and cooperative interest of everyone concerned because it has the fundamental purpose of improving the welfare of the patient. The soluton to our problem, in brief, calls for the elementary application of basic American principles of recognition for merit, consistent with the policies that have made American medicine so successful. All the suggestions proposed to solve the problems by other means have proved ineffectual in meeting the long-range needs.

To appreciate the significance and character of the changes brought about in the status of anesthesiology, it is necessary to gain a perspective of its development, particularly as it relates to care of the patient. The quality of the service rendered by the anesthesiologist to each patient is the factor that will determine the future progress of the specialty. The time is definitely past when temporary expediencies provide a satisfactory answer for poor or even mediocre anesthesia service.

CONCLUSION

In meeting the anesthesiologist's responsibility to the patient, three factors should be considered: 1. Expert anesthesia service should be available to every patient in every hospital, and providing this care is our primary responsibility. 2. The results of research and clinical investigation can be applied with full benefit to each patient only if a great many more physicians are attracted to anesthesiology. 3. Maintaining and building a better physician-patient relationship during the orderly growth of anesthesiology is the most effective way to improve the quality of anesthesia service.

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CARDIAC RESUSCITATION

Sanford E. Leeds, M.D., San Francisco

The subject of cardiac resuscitation is of great importance because delay of only a few minutes in beginning treatment may make the difference between a dead or disabled patient and a living and well one. It is important to have a predetermined plan of action and to have equipment available in order to avoid delay. Cardiac arrest or ventricular fibrillation may occur during any surgical procedure, even in a tonsillectomy with the patient under local anesthesia. It can occur during bronchoscopy or esophagoscopy; hence, anyone who performs major or minor surgery or anesthesia must be familiar with the technique of cardiac resuscitation. The cardiologist or internist who performs catheterization of the heart not only should be aware of the possibility that cardiac arrest or ventricular fibrillation may develop during the procedure but also must be prepared to treat it, since there is usually no time to call someone else to resuscitate the patient. As yet, I am not aware of any case that has developed on a hospital ward in which the patient has been successfully resuscitated.[1] This indicates the need for preparation to handle this emergency when it occurs outside of the operating room by keeping available a resuscitation kit. The kit should contain a scalpel and other instruments, some drugs with syringes and needles, a means of providing oxygen under pressure for artificial respiration, and a defibrillator. Such mobile equipment is already available in some hospitals.

There appears to be an increase in the number of patients who require resuscitation. This increase may be due to the large number of patients undergoing anesthesia, catheterization of the heart, and thoracic and, particularly, cardiac surgery. Since an effective treatment is now available, surgeons, anesthetists, members of the house staff, and others are more alert to the development of this complication and the need for treatment without delay; hence, more cases are being reported and quoted than formerly. Although "anesthetic deaths" were recognized shortly after the introduction of anesthesia 100 years ago, it is only recently that the causes of cardiac arrest and ventricular fibrillation have become better understood and a satisfactory treatment evolved. In fact, it was only five years ago that the first patient with ventricular fibrillation proved by electrocardiography was resuscitated.[2] It is now appreciated that the major causes of cardiac asystole or ventricular fibrillation are anoxia of the myocardium and reflex mechanisms[3] initiated through vagus stimulation. The best preventive is the provision of a constant stream of highly oxygenated blood through the coronary arteries. Anything that interferes with the airway or depresses respiration, such as overdosage or excessive use of multiple anesthetic agents, may bring on asystole and should be avoided.

Although the treatment of cardiac arrest and ventricular fibrillation is well established, there is much to be learned about the cause and prevention of this catastrophe. More knowledge is needed of the physiology of the myocardium, particularly with reference to the use of drugs, the magnitude and duration of the optimum electric shock needed to provide the proper "effective" current, and the factors that increase or diminish irritability of the myocardium. Because of the fortunately small number of arrests that occur (estimated at 1 in 3,000 operations[4]), it is difficult to acquire statistics regarding the effectiveness of different drugs, electrodes, or shocks under various conditions. It is, therefore, important to record carefully all observations made of clinical cases and publish them, as many hospitals are now doing. There is much information available from animal experiments in this field, and more is being accumulated, but there are certainly species differences in behavior that must be taken into account when knowledge derived from the laboratory is applied to human subjects.

Some of the facts to be acquired concern the electrical characteristics of the heart. The resistance of the dog's heart, for example, was only recently accurately measured by means of oscillographic equipment.[5] That of the living human heart has not to my knowledge been measured. Although the electric shocks and drugs that are in use are effective in most instances, it must be remembered that they have largely been determined empirically and that there is still much to be learned about cardiac resuscitation.

TECHNIQUE OF CARDIAC RESUSCITATION

When cardiac asystole develops during the induction of anesthesia or during an operation, it is usually the anesthetist who first becomes aware of the absence of the pulse and blood pressure. The surgeon can verify this quickly by noting whether there are pulsations in an artery in or near the operative field. If the heart is in the field, the surgeon may be the first to observe that it has stopped, and he may notify the anesthetist. When cardiac arrest occurs, the vital functions of circulation and respiration must be maintained artificially until the heart can resume its normal function if the patient is to survive with an intact cerebrum.

The anesthetist starts artificial respiration through a mask or endotracheal tube (preferably the latter) and supplies 100% oxygen with positive pressure. Should cardiac arrest develop on the ward or in some location away from the operating room, mouth-to-mouth forced respirations may be carried on until an anesthesia machine or other respirator can be brought to the scene.

From the Harold Brunn Institute for Cardiovascular Research, Mount Zion Hospital.

Read at the 6th Clinical Session of the American Medical Association, Denver, Dec. 5, 1952.

The studies on which this paper was based were aided by a grant from the United States Public Health Service.

1. Johnson, J., and Kirby, C. K.: The Surgical Treatment of Ventricular Fibrillation, Ann. Surg. **134**: 672, 1951.
2. Beck, C. S.; Pritchard, W. H., and Feil, H. S.: Ventricular Fibrillation of Long Duration Abolished by Electric Shock, J. A. M. A. **135**: 985 (Dec. 13) 1947.
3. Sloan, H. E.: The Vagus Nerve in Cardiac Arrest: Effect of Hypercapula, Hypoxia and Asphyxia on Reflex Inhibition of Heart, Surg., Gynec. & Obst. **91**: 257, 1950.
4. Ament, R.; Papper, E. M., and Rovenstine, E. A.: Cardiac Arrest During Anesthesia; Review of Cases, Ann. Surg. **134**: 220, 1951.
5. Mooslin, K. E.; Mackay, R. S., and Leeds, S. E.: Determination of Electrical Currents Which Will Produce Ventricular Fibrillation and Defibrillation in Dogs, presented at the Forum on Fundamental Surgical Problems, American College of Surgeons, Chicago, Oct. 18, 1949.

The anesthetist or some other person designated to perform the task keeps track of the time and notes the time at which procedures are started or drugs administered.

The surgeon may take a few seconds to prick the heart with a needle mounted on an empty syringe in order to see if it will resume a normal rhythm. Pricking the heart with a needle is indicated if asystole is present but is of no use if there is ventricular fibrillation. Since fibrillation is present in only a small percentage of cases (estimated at 10%), the maneuver is permissible but only if not more than 10 or 15 seconds are required.

After confirming the absence of arterial pulsations, the surgeon exposes the chest and makes an incision in the fourth or fifth left intercostal space reaching from the left border of the sternum to the axilla (fig. 1*A*). There is no bleeding, and the incision is quickly carried through the pleura; care should be taken to avoid injury to the left lung. The surgeon inserts his hand into the

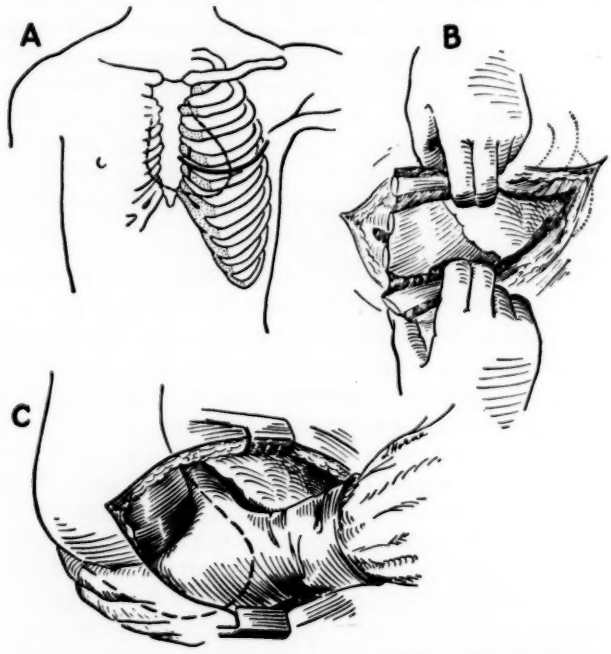

Fig. 1.—*A*, incision in fourth or fifth left intercostal space extends from the sternum to the axilla. *B*, assistant holds the ribs apart until a rib retractor is available. One or two adjacent rib cartilages may be divided to improve the exposure. *C*, surgeon grasps the heart and compresses it rhythmically 80 to 100 times per minute.

chest and starts massage. The heart is firmly squeezed in order to express as much blood as possible by each contraction of the hand. The rate of contraction should be as rapid as possible, but each contraction should be completely effective.[1] In cases in which the heart is small, as that of an infant, the rate can be maintained easily at 80 to 100 per minute, while, if the heart is larger, the rate will probably be slower. Occasionally it may be necessary to compress the heart with two hands. Effective massage is tiring and the surgeon should be relieved by an assistant so that efficiency is maintained. Proficiency in massage may be acquired by practice on experimental animals. It is easier to insert the hand into the chest if an assistant holds the fourth and fifth ribs apart until a self-retaining rib spreader can be inserted (fig. 1*B*). Additional exposure is gained if the adjacent costal cartilages are divided. If cardiac massage is not effective with the pericardium intact, the pericardium should be opened so that the surgeon may better grasp the ventricles with his hand. Should bleeding from the chest wall occur during massage of the heart, the assistant may clamp and tie the vessels. The skin may be painted with an antiseptic solution, and sterile towels may be applied after massage is initiated.

The need for haste is plain. The anesthetist or surgeon may not discover the absence of arterial pulsations for a minute or more. It has been determined experimentally [6] that the central nervous system is damaged after four to six minutes of anoxemia. A rule of thumb is that the circulation and respiration must be started artificially before two or three minutes have elapsed if the patient is to survive without damage to the brain.

Once respiration and circulation are maintained artificially, the patient's condition improves, the pulse and blood pressure are obtainable, and there is no longer need for haste. A case was reported by Beck [2] in which massage was carried on for an hour before the heart resumed its normal function; no permanent injury to the heart occurred. One may look for ventricular fibrillation at this time. The worm-like contractions of the myocardium may be seen through the thin pericardium, or, if there is any doubt, the pericardium may be opened.

While respirations and cardiac massage are being maintained, fluids, such as a solution of 5% dextrose in distilled water or blood, should be administered intravenously. These fluids will increase the return of venous blood to the heart and support the circulation.

The next problem confronting the resuscitation team is that of returning the heart to a normal rhythm. When the heart is in asystole, it may stay in that condition for a variable length of time. According to present knowledge, it will either return to normal rhythm or change to ventricular fibrillation. If the heart returns to a normal rhythm that is weak with poor contractions, epinephrine should be given in amounts of 0.5 to 1 cc. of a solution made by mixing 1 cc. of a 1:1000 solution with 4 cc. of isotonic sodium chloride solution. This preparation should be injected into the auricle, and injection may be repeated every three minutes. If the heart remains in asystole for 5 or 10 minutes and appears to be losing its tone, epinephrine or calcium chloride may be administered very cautiously in small dosage, since ventricular fibrillation may develop if the irritability of the myocardium is increased. Procaine hydrochloride and procaine amide (Pronestyl) hydrochloride are contraindicated in asystole because they may further depress a myocardium that is not contracting. In adults, atropine should be administered intravenously in amounts of 0.01 grain (0.6 mg.), especially in cases in which the vagovagal reflex appears to be responsible for the arrest.

Mention should be made of the drugs that are useless or contraindicated in cardiac resuscitation. Analeptic and sympathomimetic drugs, such as caffeine, nikethamide (Coramine), pentylenetetrazol (Metrazole), strychnine, ephedrine, amphetamine (Benzedrine), phenylephrine (Neo-Synephrine) hydrochloride, and *p*-(2-aminopropyl) phenol (Paredrine), should not be

6. Weinberger, L. M.; Gibbon, M. H., and Gibbon, J. H., Jr.: Temporary Arrest of the Circulation to the Central Nervous System: I. Physiologic Effects, Arch. Neurol. & Psychiat. 43: 615 (April) 1940.

used. Drugs that stimulate the central nervous system increase the oxygen demand; in cases in which there is anoxia, the danger of damage is aggravated. Medicaments such as digitalis and strophanthin act on the auriculoventricular conduction system to increase the refractory period and to slow the rate of conduction; they should also be avoided.

Should ventricular fibrillation develop, single or serial shocks may be applied with the defibrillator prior to the administration of procaine. Should the shocks fail to produce a normal rhythm, procaine or procaine amide hydrochloride should be given to aid in defibrillation. Procaine hydrochloride is administered, 10 cc. of a 1% solution, into the auricle; 200 mg. of procaine amide hydrochloride should be administered either intravenously or directly into the auricle. Ventricular fibrillation may revert to a normal rhythm with massage pressed firmly against the heart, the shocks are more likely to be effective, since an adequate current will pass through the heart.

It has been shown [8] that weak currents below 55 volts and 1 ampere administered to the heart of a normal dog will result in ventricular fibrillation. An effective and safe defibrillating current must be above 55 volts, preferably nearer 110 volts and 2 amperes, if the drop in voltage and amperage across the electrodes caused by the resistance of the tissues or by contacts is not to act as a fibrillating current. For these reasons, voltages below 70 or 80 are extremely dangerous and should not be delivered by any defibrillator intended for use in hospitals. If a timer is incorporated in the defibrillator so that currents lasting 0.1 or 0.5 second are used (preferably the former), no burn will occur even in an infant's heart.

Drugs That Are Useful in Cardiac Resuscitation

Drug	Dosage	Indications	Contraindications	Remarks
Epinephrine	0.5 to 2 cc. 1:5,000 solution in auricle	Regular rhythm; weak contractions; cautiously in asystole	Ventricular fibrillation present	Stimulates heart by direct effect on myocardium and conduction system; increases myocardial irritability
Calcium chloride	2 to 4 cc. 10% solution in left ventricle	Regular rhythm; weak contractions; cautiously in asystole	Ventricular fibrillation present	Will sometimes revive heart that does not respond to epinephrine *
Procaine hydrochloride	10 cc. 1% solution in auricle or 50 to 100 cc. 1% solution intravenously	Ventricular fibrillation that fails to respond to shocks	Asystole present and myocardium flabby	Diminishes irritability of myocardium and conduction system
Procaine amide hydrochloride (Pronestyl)	100 to 200 mg. in auricle or intravenously	Ventricular fibrillation that fails to respond to shocks	Asystole present and myocardium flabby	Diminishes irritability of myocardium and conduction system
Atropine and scopolamine	.0065 gm. or 0.01 grain intravenously	Cardiac arrest due to vagovagal reflex	Tachycardia present	Block vagal effects on sinoauricular pacemaker
Quinidine	0.2 gm. 4 or 5 times daily, orally	Presence of cardiac arrhythmia preoperatively	Intravenous or intracardiac use	Decreases myocardial excitability and slows conduction of impulses
Barium chloride	1 to 2 cc. 0.5% solution	Regular rhythm; weak contractions; cautiously in asystole	Ventricular fibrillation present	Used less frequently than calcium chloride
Potassium chloride	0.5 to 5% solution	Ventricular fibrillation; to produce cardiac inhibition	Asystole present or regular contractions weak	Not recommended; electrical defibrillation is probably more efficient and less dangerous

* Kay, J. H., and Blalock, A.: The Use of Calcium Chloride in the Treatment of Cardiac Arrest in Patients, Surg., Gynec. & Obst. **93**: 97, 1951.

alone [7] in human patients. It is doubtful whether this reversion occurs in dogs in which fibrillation has been produced by a weak electric shock. After the administration of procaine or procaine amide hydrochloride electric shocks are again administered with the defibrillator. The defibrillator can be constructed to deliver a shock of 110 volts or 130 volts with a timer that allows the administration of voltages of 0.1 second duration. In order to avoid or minimize damage to the myocardium from burns or other effects, a shock of 110 volts for 0.1 second is given first. If single shocks at the lower voltage are not effective, 5 to 10 serial shocks at one second intervals are administered. The higher voltage of 130 is used if a shock of 110 volts is not effective. If poor contact is made while employing very small electrodes, a shock of even 130 volts may be inadequate because of the high resistance present in the circuit. It is evident that the electrodes and their contact are extremely important. If the pericardium is open and electrodes covered with gauze moistened with sodium chloride solution are

The defibrillating current is effective because it produces cardiac arrest that may be followed by a normal rhythm. By passing a strong shock through the myocardium, all the wayward contractions of the myocardium are stopped, and, once a regular rhythm is resumed, the contractions may be improved, if weak, by the administration of epinephrine. After the heart has resumed a normal rhythm, the chest is closed with absorbable surgical sutures. An underwater seal drain may be used. Oxygen is administered as needed and antibiotics are employed for several days.

THE DEFIBRILLATOR

In order to construct an effective defibrillator, certain basic facts must be known regarding the effects of electric shocks on the heart. Much information has been gained

7. Lampson, R. S.; Schaeffer, W. C., and Lincoln, J. R.: Acute Circulatory Arrest from Ventricular Fibrillation for 27 Minutes, with Complete Recovery, J. A. M. A. **137**: 1575 (Aug. 28) 1948.

8. Leeds, S. E.; Mackay, E. S., and Mooslin, K. E.: Production of Ventricular Fibrillation and Defibrillation in Dogs by Means of Accurately Measured Shocks Across Exposed Heart, Am. J. Physiol. **165**: 179, 1951.

from experiments on dogs.[9] As more data are acquired from cardiac resuscitation in human subjects, the technique may require some modification.

The range of effective voltages and amperages must be known so that only effective currents are delivered to the myocardium. By "effective current" is meant current that actually traverses the myocardium, not current that is delivered by the defibrillator when the electrodes are in direct contact with each other and meet only minimal resistance. Below about 55 volts and 1 ampere, the shock

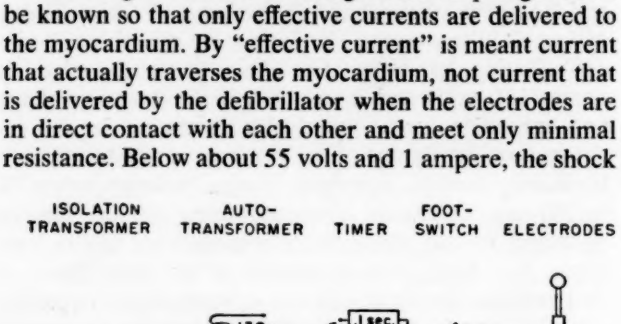

Fig. 2.—Defibrillator including the important component parts.

may produce fibrillation in a heart that is beating normally. Weak currents long enough in duration to span an entire cardiac cycle will usually produce fibrillation in both dogs and humans. In order to produce defibrillation, the current must be higher than 55 volts and 1 ampere (demonstrated in dogs). Very strong currents will defibrillate satisfactorily but may burn or otherwise injure the heart; therefore, a current must be selected that will be high enough to be effective but not so high that it will be injurious. Another factor to be considered is the duration of the shock. Weak shocks, if very short (0.1 second or less), will not always cause fibrillation when applied to a heart with a normal rhythm, because they may occur during the refractory period of the cycle in which the shock is not effective. To produce fibrillation, therefore, weak shocks that last through one or more cardiac cycles (0.5 to 1.0 second) should be used. The reverse is true when the optimum duration of a defibrillating current is selected. If defibrillation is desired, both long and short currents are equally effective, but long currents may damage the heart; hence, the shortest current that is effective should be used. It has been determined experimentally that brief currents lasting from 0.1 to 0.5 second are effective and are less apt to cause burns. Wiggers [10] showed that, if single shocks do not result in defibrillation, serial shocks should be used. Five to 10 serial shocks administered for 0.1 second at one second intervals may be successful at times at which a single shock fails. This has been explained by the fact that isolated islands of fibrillation in the myocardium may persist after a single shock but that, after several shocks, the entire myocardium is arrested.

In a discussion of defibrillation, the final and one of the most important factors to be considered is the electrodes. The electrodes should be as large as can conveniently be placed on the heart so that local heating is minimized and contact resistance is reduced. They should be covered with felt or gauze that may be saturated with sodium chloride solution in order to improve conduction. In order to make the contact as good as possible, the electrodes should be held firmly against the heart on opposite sides of the ventricles. The handles and shafts should be well insulated so that the person holding the electrodes will not receive an accidental shock and so that sparks will not be produced in the operating room. As a further precaution, the back of each electrode should be insulated. In order to avoid shocks to personnel, it is wise for each electrode to be held by a different person each wearing rubber gloves and standing on a dry floor away from the metal operating table. In this way it is almost impossible for them to receive a shock, especially if, in addition, an isolation transformer is used in the circuit of the defibrillator. By using an isolation transformer, a shock could be received only through contact with both electrodes simultaneously during the short period of time that the relay is closed.

The parts of an ideal defibrillator are determined from considerations mentioned earlier in this paper; first, an isolation transformer should be included, since this safety device makes it practically impossible for the person holding an electrode to receive a shock, and, second, the voltages available should be considered. Probably, the minimum voltage should be 110, as use of voltages below this value, even in infants, may result in a fibrillating current if the resistances across the electrodes are too high. The maximum voltage required should be about from 130 to 150 volts. If the defibrillator is built to deliver only one voltage, 130 volts would be the most desirable. With a thorough recognition of the need for large electrodes applied firmly with good contact through saline

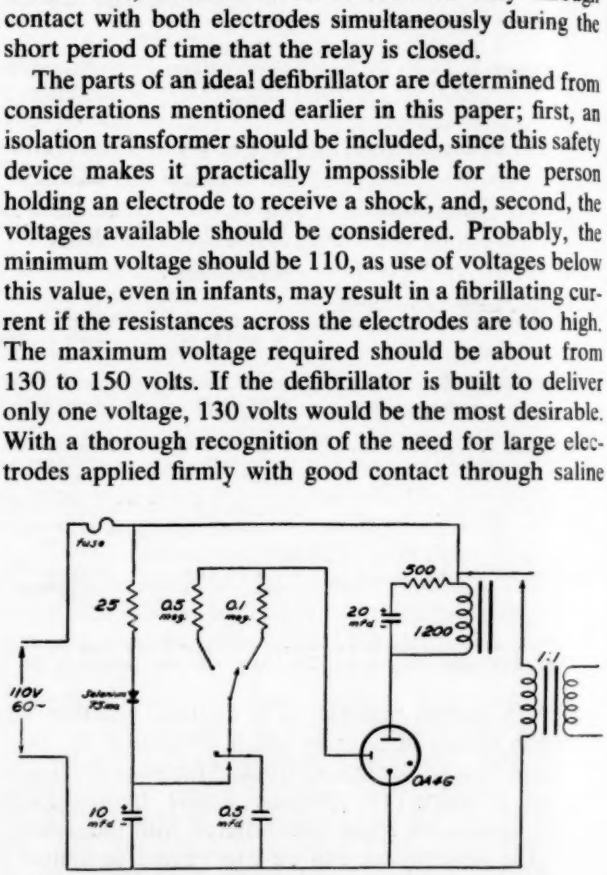

Fig. 3.—Defibrillator circuit devised by Dr. R. S. Mackay. Reproduced from Mackay, R. S.; Moaslin, K. E., and Leeds, S. E.: The Effects of Electric Currents on the Canine Heart with Particular Reference to Ventricular Fibrillation, *Ann. Surg.* **134**: 173 (Aug.) 1951.

soaked material, it would appear unnecessary to use voltages higher than 130. If the available electrodes are small, voltages up to 150 might be necessary. If defibrillation does not occur when a shock of 130 volts is administered, it is probably wiser to open the pericardium and to make good contact than to apply extremely high voltages, which in themselves may be harmful to the patient. The limit of 150 volts is arbitrary. Actually the type of study that would determine this figure accurately has not been carried out in human subjects thus far.

9. Mackay, R. S.; Mooslin, K. E., and Leeds, S. E.: The Effects of Electric Currents on the Canine Heart with Particular Reference to Ventricular Fibrillation, Ann. Surg. **134**: 173, 1951. Mooslin, Mackay, and Leeds.[5] Leeds, Mackay, and Mooslin.[8]

10. Wiggers, C. J.: The Physiologic Basis for Cardiac Resuscitation from Ventricular Fibrillation—Method for Serial Defibrillation, Am. Heart J. **20**: 413, 1940.

As a third part, the ideal defibrillator should include an automatic timer. This is not difficult to construct, and its use is far superior to estimation of the duration of shocks during the sometimes hectic process of cardiac resuscitation. The timer may be set at 0.1 or 0.2 second; longer periods up to 0.5 second are satisfactory but probably not necessary.

Fourth, a foot switch is necessary. The type of switch that discharges the entire shock when the switch is depressed is most satisfactory. As stated above, it is best for the shock to be timed automatically and discharged completely when the switch is stepped on. A spring sets the switch for the next shock as soon as the foot is lifted.

Fifth, the design of the electrodes must be considered. The impression is that any good conductor may be used. Several sizes should be available so that the heart of an infant or of an adult may be accommodated. The smallest should be 5 cm. in diameter and the largest 8 cm. in diameter. The insulation of the handle, shaft, and cord should be adequate to withstand autoclaving. An additional precaution is insulation of the back of each electrode. The electrodes may be covered with felt or they may be wrapped with flat gauze sponges that are tied in place. The felt or gauze should be moistened well with sodium chloride solution before the electrodes are applied to the heart. The defibrillator that has been described is illustrated in figure 2. Diagrams of two different, practical defibrillators are in figures 3 and 4.

RESUSCITATION KIT AND ITS ADJUNCTS

The instruments and drugs necessary or useful in cardiac resuscitation are listed in outline form.

I. Equipment required immediately for establishment of circulation and respiration
   - A. Instruments for exposure of the heart; scalpel and self-retaining rib retractor
   - B. Oxygen tank with bag and couplings that connect to a tight fitting face mask (preferably with airway). Laryngoscope, mouth gag, and intratracheal catheters and airways of different sizes may be needed
   - C. Kreiselman apparatus should be available in all operating rooms if above equipment is not

II. Equipment required after circulation and respiration are established by artificial means
   - A. Skin antiseptics and sterile towels, drapes, and gloves
   - B. Instruments to control bleeding from chest wound when pulse and blood pressure have returned; hemostats, absorbable surgical sutures, forceps, and scissors
   - C. Instruments to open pericardium if necessary to improve massage, verify presence or absence of ventricular fibrillation, or to permit application of electrodes directly to the epicardium; long forceps with teeth and long scissors
   - D. Drugs
     1. Procaine hydrochloride, 1% solution
     2. Epinephrine, 1:5,000 solution
     3. Calcium chloride, 10% solution
     4. Procaine amide hydrochloride (Pronestyl)
     5. Atropine
   - E. Syringes with needles
   - F. Defibrillator unit including sterile electrodes covered with gauze or felt and connecting wires
   - G. Instruments, suture material, and catheter to be used in closing the thoracotomy wound

The defibrillator and a sterile pack containing electrodes and connecting wires are the last items that must be available. Although a scalpel and rib spreader could be kept in readiness on each ward or in each minor operating room, it would not be practical to have a respirator or anesthesia machine and a defibrillator in every location in which it might be needed. It would seem wise to keep a complete resuscitation kit and adjunct equipment in readiness at some central point and to depend on mouth-to-mouth breathing to maintain respirations until the equipment can be brought to the patient.

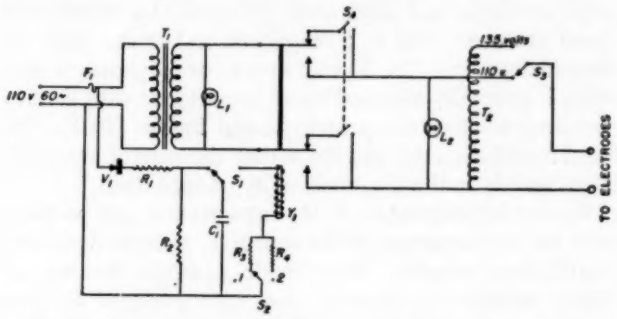

Fig. 4.—Defibrillator circuit devised by Mr. Richard Wexler. This circuit does not contain a vacuum tube.

SUMMARY

1. A technique of cardiac resuscitation is described in detail that includes (*a*) artificial respiration, (*b*) cardiac massage, (*c*) administration of fluids and blood intravenously if indicated, (*d*) administration of drugs, such as epinephrine, calcium chloride, procaine and procaine amide (Pronestyl) hydrochloride, and atropine, and (*e*) defibrillation by means of electric shock.

2. The defibrillator is described in detail. Construction of the defibrillator is discussed with regard to the effects of electric current on the heart. Circuit diagrams of defibrillators are included.

3. An outline of equipment required for cardiac resuscitation based on the technique described is presented. This list is designed to assist in preparation of the resuscitation kit and adjunct equipment.

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Narcotics and Cancer.—The cancer patient presents a unique problem to the doctor who is called upon to decide when and what pain relieving drugs should be administered. . . . Since patients with cancer are always more or less mentally depressed and subject to periods of despondency, they are much more prone to develop dependency and habituation than are the usual surgical and medical patients. Since this is true, sedation and narcosis when needed as a temporary measure should, if possible, be accomplished by drugs having the minimal amount of habit forming qualities. Following surgery, if morphine or Pantopon must be used, their use should be discontinued as soon as possible. Where narcotics must be continued for a considerable period of time, codeine or Demerol may be satisfactorily substituted for morphine. This will make the discontinuance of narcosis much easier for both the patient and the doctor. Discomfort and mild pain during the course of treatment are best handled with non-narcotic drugs, such as aspirin, acetanilide, and barbiturates, either separately or in combination. Larger doses of aspirin than are usually given when repeated at regular intervals will prove more effective than is usually believed.—E. Callaway, M.D., Narcotics and Cancer, *Georgia Medical Association Journal*, May, 1953.

EVALUATION OF A THYROID PANEL

PRACTICAL APPLICATION OF SCINTILLATION COUNTER IN DIAGNOSIS OF DISEASES OF THE THYROID

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Since I^{131}, the eight day, half-life isotope of iodine, became available on a large scale, its uptake by the thyroid gland has been used as a diagnostic test in the study of thyroid disorders. The thyroid uptake or diagnostic tracer study is generally afforded equal importance with the determination of serum protein-bound iodine (PBI), the basal metabolic rate, and the serum cholesterol level, the latter mainly in the diagnosis of hypothyroidism.

Recent improvements in instrumentation and particularly the development of the sensitive, gamma detecting scintillation counter [1] have made possible the use of tracer amounts as small as one microcurie of I^{131} for studying thyroid function. This amount is about one-hundreth of the dose that has been commonly used in the past and makes it possible, for the first time, to obtain repeat uptake values without exceeding a safe dosage level. This simple and reliable equipment, which is now commercially available,* makes possible the expeditious processing of a large number of patients in a thyroid diagnostic clinic. The uptake procedure outlined in this report can be carried out by a technician. Many other methods utilizing I^{131} have been suggested for determining thyroid function,[2] but many of these are too complex to be carried out in a simple and rapid manner in a thyroid clinic.

This report presents the results of a pilot study designed to evaluate the I^{131} tracer test (thyroid uptake) in a large Veterans Administration general medical and surgical hospital in which the patients are, for the most part, men. The hospital is located in an area in which goiter is not endemic.

METHODS

The instrumentation has already been described in detail.[3] Briefly, standardized doses of 2 μc of carrier-free I^{131} are prepared in capsule form.[4] The use of the dosage in capsule form has a number of advantages, particularly with respect to the ease of transportation from the standardization laboratory to the patient and the elimination of possible contamination through spillage. The patient is permitted a light breakfast and is given the I^{131} capsule with a small amount of tap water. Uptake studies are performed 6 and 24 hours after administration of the dose. The determination of the amount of I^{131} collected by the thyroid gland is carried out as follows: The patient is seated in a dental chair, and the chair is titled backward so that the patient's neck is in a horizontal position. The isthmus of the thyroid gland is located by measuring 5 cm. downward from the notch of the thyroid cartilage. The scintillation tube is then lowered over the thyroid area so that the center of the aluminum window of the tube is 5.6 cm. above the isthmus. Background counts are obtained over the knee and are subtracted from the thyroid counts to obtain the net count over the thyroid. This net count is expressed as a per cent of the administered dose count obtained under the same geometric conditions and represents the per cent uptake by the gland. A request slip should accompany the patient and should state the reason for which the test was requested, the tentative clinical diagnosis, and all medication that the patient has been receiving. Every effort is made to determine whether or not the patient has received desiccated thyroid, iodine containing medication, or iodized oils used in roentgenographic diagnosis, since these markedly modify the thyroid uptake.

It is emphasized that no pressure whatsoever was placed on the house staff for the referral of patients. At the time this pilot study was established, members of the house staff were encouraged to avail themselves of the facilities of the thyroid diagnostic clinic at their discretion. Patients in whom there was doubt as to the presence of thyroid dysfunction were referred. These included patients with symptoms such as nervousness, tiredness, and unexplained weight loss or weight gain. Also included were patients with heart disease of unexplained cause and brittle diabetics. Each of the house officers or attending physicians was thus a referring physician, and the situation was comparable to the relationship of private physician to a commercial laboratory. This method was felt to be vastly preferable to one in which only one physician examines all patients to be tested and the clinical impression depends on his index of suspicion and clinical acumen.[2b]

Basal metabolic rate, serum protein-bound iodine, and serum cholesterol determinations, according to the techniques of Barker and Humphrey [5] and Kingsley and Schaffert,[6] were performed at the same time or a few days after the I^{131} tracer test. The results obtained are analyzed with respect to: (1) accuracy of the tracer study as a routine clinical test to supplement the referring physician's clinical impression; (2) comparative diagnostic value of the tracer study and the other established thyroid function tests; (3) simplicity, practicability, and possible application of the tracer study in smaller hospitals to the exclusion of some of the other thyroid function tests.

Because of lack of space, some of the bibliographic footnotes have been omitted from THE JOURNAL and will appear in the authors' reprints.

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MATERIAL

One hundred sixteen healthy control subjects were given an oral tracer dose of 2 μc of carrier-free I^{131}. The range of uptake values (7% to 23% in 6 hours and 12% to 35% in 24 hours) correlates well with those found by other groups of investigators [7] (table 1). As illustrated in table 1, 273 tests were performed on 213 patients. Of these 273 tracer studies, there were 195 normal tests and 78 abnormal tests, according to our criteria. The breakdown of these abnormal tests reveals that 17 were higher and 61 lower than the normal control values. The breakdown of the tests with values above normal (tables 2 and 3) shows that all but one can be explained on the basis of hyperthyroidism. The one patient (patient 17, table 3) with uptakes of 44% and 46% had normal protein-bound iodine and high serum cholesterol values. He suffered from hypertensive cardiovascular disease and had had a cerebral vascular accident. He was also in cardiac decompensation, on a low sodium diet, and receiving digitalis. Clinically, there was no evidence of hyperthyroidism. He had received potassium thiocyanate tablets two months prior to the test, but whether this accounts for the high uptake cannot be stated definitely. The rate of uptake in the same patient, as evidenced by the six hour determination, was normal. In this series of patients, no other high uptake that could not be explained was found.

TABLE 1.—*Results of Radioactive Iodine Uptake Tests*

	Men	Women	Total
Voluntary healthy controls	55	61	116
Number of patients	165	48	213
Number of tests on patients	211	62	273
Number of tests within normal range	147	48	195
Number of tests outside normal range (7 to 23% at 6 hr. 12 to 35% at 24 hr.)	64	14	78
Above normal	16	1	17
Below normal	48	13	61

The breakdown of low uptakes is given in tables 4 and 5. False low values due to "contamination" of the patient with thyroid medication or iodine containing compounds were more frequent than those due to hypothyroidism, adenomas, or thyroiditis. The factors responsible for uptake values below normal included thyroid medication (11 patients), iodine in Lugol's solution, potassium iodide, hydriodic acid, kelp, patent medicine tonics, and cough syrups (9 patients), dyes used in roentgenographic procedures (4 patients), and iodochlorohydroxyquinoline (Vioform) (1 patient). One patient with bromide intoxication had a low uptake and a high bromide level in the serum. Unfortunately, this patient failed to return for a repeat tracer study several weeks later. In several patients with congestive heart failure, it was observed that, although the total amount of I^{131} accumulated in the thyroid gland was within the normal range, the rate of uptake was slow (six hour determination). These are preliminary observations that are being studied further.

TABLE 2.—*Presumptive and Definitive Diagnosis in Patients with Abnormally High Uptakes*

Presumptive Diagnosis	Definitive Diagnosis	No. Patients
Hyperthyroidism		
Unequivocal	Hyperthyroidism	6
Probable or possible	Hyperthyroidism	5
Heart disease		
Type undetermined	Toxic adenoma, thyrocardiac	1
Type undetermined	Hyperthyroidism, thyrocardiac	4
Type undetermined	Hypertensive heart disease, possible distortion by KSCN	1
		17

TABLE 3.—*Comparison of Laboratory Findings in Seventeen Patients with Abnormally High I^{131} Uptakes*

Patient	Uptake, % 6 Hr.	Uptake, % 24 Hr.	Basal Metabolic Rate, %	Protein-Bound Iodine, μg per 100 Cc.	Cholesterol, Mg. per 100 Cc.
1	46	53	+21	5.1	110
2	49	54	+47	10.6	137
3	29	42	.....	4.9	143
4	26	40	+17	11.5	229
5	41	55	+28	11.8	178
6	48	59	+68	12	131
7	65	65	+43	12.6	142
8	45	58	+40	8.4	217
9	35	47	+15	7.7	150
10	44	55	+15	18	171
11	32	43	.....	8	...
12	35	48	+8	8.4	143
13	50	58	+20	10.1	206
14	36	50	+8	9.8	138
15	24	52	+12	12.7	182
16	34	57	+37	7.9	151
17	(1) 21	44	.....	5	206
	(2) 22	46	.....	4	258

A number of uptake values were found to be at the lower range of normal, such as 10 to 12% in 24 hours. No satisfactory explanation can be offered for this finding in persons in whom the results of other laboratory tests were all within the normal range. Several such patients were referred to the thyroid clinic a few days after a surgical procedure. The lowered thyroid uptake might be explained on the basis of surgical trauma, such as that demonstrated by Blount and Hardy.[8] Whether other uptake values are due to nonspecific stress is mere speculation. It is emphasized, however, that these uptake values slightly lower than normal are not to be considered as being in the hypothyroid range. On the contrary, after examining these persons, it was found that the diagnosis made by the referring physician was possible hyperthyroidism, anxiety state, et cetera.

RESULTS

The following comparisons between the I^{131} tracer test, basal metabolic rate, serum protein-bound iodine, and serum cholesterol as indexes of thyroid function may be made as a result of this study.

TABLE 4.—*Causes of Low Radioactive Iodine Uptake*

Cause of Low Uptake	No. of Patients
Myxedema	10
Hypothyroidism after thyroidectomy or I^{131} therapy	4
Thyroiditis	5
Cortisone therapy	3
Thyroid adenoma, nontoxic	8
"False low"	28
Unexplained	3
	61

It is generally agreed that the basal metabolic rate correlates reasonably well with results of the tracer test in unequivocal cases of hyperthyroidism or hypothyroid-

ism; however, its wide fluctuation in euthyroid persons limits its usefulness. Hyperthyroidism without apparent hypermetabolism has been described.[9] In such cases, the basal metabolic rate is normal, but the I^{131} uptake and the serum protein-bound iodine level are elevated. No such person was observed in our series. The tracer test as compared with determination of the basal metabolic rate has the advantage that the patient's cooperation is unnecessary. The tracer test is an outpatient test, since a period of rest is not necessary before the test. A combination of a high basal metabolic rate and a depressed uptake has been mentioned in factitious hyperthyroidism caused by secret thyroid medication.[10] No such case has come to our attention.

The serum cholesterol determination is valuable in patients with hypothyroidism but not in patients with hyperthyroidism.[2b]

The results of protein-bound iodine determination and of the tracer study compare very well in most instances.

TABLE 5.—*Comparison of Laboratory Findings in Fourteen Patients with Abnormally Low I^{131} Uptakes*

Patient	Diagnosis	24 Hr. Uptake, %	Basal Metabolic Rate, %	Protein-Bound Iodine, μg per 100 Cc.	Cholesterol, Mg. per 100 Cc.
1	Pituitary myxedema	2	— 28	6.8	384
2	Myxedema	0.6	— 15	4	245
3	Postoperative myxedema	7.3	— 6	7.1	501
4	Myxedema	1	.....	5.1	349
5	Postoperative myxedema	2	— 18	4.6	213
6	Postoperative myxedema	2	.....	...	...
7	Postoperative myxedema	6.3	— 18	3.7	503
8	Hypothyroidism after I^{131} therapy	10	.....	4.2	340
9	Myxedema	1.5	— 23	5.8	467
10	Myxedema	1	— 35	3.6	536
11	Rheumatoid arthritis *	6	— 3	5	263
12	Dermatitis *	6	— 5	4.8	178
13	Dermatitis *	10	— 13	4.7	116
14	Malignant hypertension, probable hypothyroidism	2	— 34	7.1	205

* Patient receiving cortisone.

Our own experience confirms the observation that the combination of these two procedures is probably the best available laboratory tool for confirmation of the clinical impression of thyroid disease.[11] It can be seen from tables 1, 2, and 3 that, in all patients with hyperthyroidism, the two tests were diagnostic. It can be argued that only one of the two tests is necessary, but it is in the patient with suspected hypothyroidism that the two procedures are of great value. Low uptake and low protein-bound iodine level are normally found in hypothyroid persons. The uptake test is more sensitive than the determination of protein-bound iodine level in such cases, since, even in cases of full blown myxedema, a protein-bound iodine level of 4 μg per 100 cc. is not uncommon. If 5 to 7 μg per 100 cc. is the normal value, then it is readily apparent that the value of 4 μg per 100 cc. are not too helpful. The combination of a low uptake and a high level of protein-bound iodine indicates, in our experience at least, premedication with iodides; only the pattern of thyroiditis is similar. It has been our practice to elicit from the patient an exhaustive history with regard to the intake of compounds containing iodine. In almost every instance of low uptake and high protein-bound iodine level, this was found. Repeat uptake tests were performed in such instances, but at this time it cannot be stated how much time should elapse before such tests are accepted as truly diagnostic.

It is of interest to note the large number of patients who were taking thyroid medication. This depressed the uptake in almost every instance but usually did not raise the protein-bound iodine level significantly. In any patient who is receiving desiccated thyroid medication, it has been our practice to do the I^{131} uptake test and then repeat it three weeks later. Our data bear out the observations of Greer [12] who found that the uptake returns to normal in about three weeks after discontinuation of thyroid medication. Unpublished preliminary observations from this laboratory indicate, however, that the values obtained after three weeks may be abnormally high. Thus serial tracer studies made three weeks apart for several months indicate that a definite rebound phenomenon follows cessation of thyroid medication before the uptake values return to a normal pattern.

Attention is directed to the observation that of the 16 patients with hyperthyroidism only 6 diagnoses were clinically unequivocal. In five of the remaining cases, the primary diagnosis was heart failure of unexplained cause; in the other five, the diagnosis was suspected but confirmation was necessary before treatment could be instituted. All of the 16 persons with hyperthyroidism were treated and have improved, thus giving final proof of the accuracy of the laboratory tests. No patient with proved hyperthyroidism was found to have a normal or low uptake value.

The patients with full blown myxedema were all diagnosed without hesitation; the laboratory studies merely confirmed the clinical impression. Hypothyroidism was suspected in more persons in whom results of the tracer study turned out to be normal than in those with hyperthyroidism. The five patients with thyroiditis were all followed up after their disease had subsided and showed a normal uptake and protein-bound iodine value several weeks after the original tests. In three, the referring diagnosis was hyperthyroidism; only in the remaining two was thyroiditis considered. One patient with carcinoma of the thyroid gland had a normal uptake.

COMMENT

In our experience, the radioiodine thyroid uptake test is an accurate, sensitive, and practical laboratory aid in the diagnosis of thyroid disorders. The test is safe and rapid. It requires no special preparation of the patient, and the patient's undivided attention and cooperation are not necessary, as in the determination of the basal metabolic rate. A technician can do the test accurately, since the operation of the counting equipment is very simple. Since tracer doses of I^{131} can now be obtained commercially, close association with a radioisotope laboratory is not necessary. This is an advantage over the protein-bound iodine determination that must be done by specially trained technicians and with special equipment. In this study, one of us (S. R. J.) took

charge of the thyroid diagnostic clinic because it was felt that only very careful examination of the patient's record would give information concerning premedication with iodized compounds, thyroid, and roentgenographic contrast mediums. This was eminently successful as every patient's record was examined, every patient was questioned with regard to premedication, and many cases of contamination were discovered to explain false low uptake values. As a routine procedure, however, it is felt that any technician can operate such a thyroid tracer laboratory under the supervision of a physician.

It should be emphasized that the I^{131} uptake test may not be the ideal thyroid function test and that it is not necessarily better than the determination of the protein-bound iodine level. It measures the avidity of the thyroid gland for iodine and is subject to the same errors as is the serum protein-bound iodine determination. These pitfalls are usually due to iodine or thyroid medication and should be attributed to "patient error" rather than to failure of the tests.

A great number of variants of the simple direct measurement of I^{131} over the thyroid gland have been described.[13] None of these methods fulfill the criteria for the ideal thyroid function test, and they are too complicated to be used as routine tests in a general hospital without close association of a radioisotope laboratory.

The 6 hour uptake and 24 hour uptake determinations are practical, since the 6 hour determination measures the rate of I^{131} accumulation by the thyroid gland and the 24 hour determination measures the approximate maximum concentration. The reasons for this have been described elsewhere.[14] It is the feeling in this laboratory that a 24 hour uptake test alone is sufficient for screening purposes but that much valuable information can be gained by obtaining an earlier determination such as one at 6 hours.

SUMMARY

The results of a pilot study of four thyroid function tests (basal metabolic rate, protein-bound iodine and serum cholesterol determinations, and radioactive tracer test) in a Veterans Administration hospital are reported. The radioactive iodine tracer test was performed with doses of 2 μc of I^{131}, administered in capsule form to control subjects and to patients suspected of having thyroid disorders. A scintillation counter was used to measure the uptake of I^{131} by the thyroid gland.

The radioactive iodine tracer test, using small doses of radioactive iodine and the scintillation counter, is a practical test and compares favorably with determination of the basal metabolic rate and protein-bound iodine and serum cholesterol levels. The combination of the protein-bound iodine test and the radioactive iodine tracer test is an excellent laboratory tool for confirmation of the clinical impression of thyroid disease. The radioactive iodine tracer test is sensitive and is probably the best available thyroid function test. The test can be performed by a trained technician with commercially available radioactive iodine and scintillation counter equipment.

The results of these four tests (basal metabolic rate, protein-bound iodine and serum cholesterol determinations, and radioactive iodine tracer test) in a series of unselected patients are presented and discussed.

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THE ROLE OF EMOTIONS IN DERMATOSES

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The skin may reveal emotional states as eloquently as do the muscles of facial expression. Control of facial muscles may keep the visage inscrutable despite inner turmoil; but voluntary control is useless in suppressing the blush of embarrassment or the cold sweat of fear. Our daily conversation is replete with references to revelations of feelings on the integument. We speak of the face that becomes "purple with rage" or "white with fear." The person impervious to insult is referred to as "thick-skinned"; the sensitive one is "thin-skinned." Aware of danger, one's "hair stands on end"; he may "bristle with courage" or, frozen with fright, have cutis anserina ("goose flesh"). We refer to the "sweating-out" of an unpleasant situation. The expression to "sweat blood" finds its origin in purpuras and religious stigmas of hysterical origin.[1] The term "a blistering denunciation" is derived from the ability to produce blisters by hypnotic suggestion; the intensity of induced blisters may fluctuate with the emotional state of the subject.[2]

Sensory disturbances of the skin are also induced by emotions. Thus one "tingles" with expectation or is "tickled" by an amusing incident. Hostility may cause us to "itch for revenge." A repulsive sight makes our skin "crawl" or gives us the "creeps," the very sensations of patients afflicted with delusions of parasitosis. Fearful of a venture, we speak of getting "cold feet." We are "sitting on pins and needles" while awaiting an important decision—a preface to anal and genital pruritus. The symbolism expressed by excoriations has its parallel in the remark "stop picking on me."

The purpose of this paper is to examine the emotions responsible for changes in the skin; to describe the physical agencies through which they mediate these effects; and to discuss diseases of the skin that appear to have important emotional components.

EMOTIONAL COMPONENTS OF PSYCHOSOMATIC DERMATOSIS

English [3] describes eight common emotions, some of which are conspicuous in the personalities of patients with certain skin disorders. It is, therefore, of practical importance to investigate these emotions.

The need for love is one of humanity's greatest hungers.[3] If this hunger is unsatisfied, the resulting

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frustration may lead to other unpleasant emotions. The person who believes himself unloved may resort to symbolic or perverted ways of obtaining affection. If these substitutes overflow into the autonomic nervous system, there is consequent itching and scratching. Thus certain skin diseases, especially localized neurodermatitis and anogenital pruritus, may be unconscious erotic substitutes for a lack of love.

Yaskin [4] states that anxiety is the central symptom of nearly all the psychoneuroses. One may be consciously aware of anxiety as feelings of fear and worry. If the causes of the anxiety are below the level of consciousness, however, an overflow into autonomic pathways commonly occurs, and bodily dysfunctions, including skin disorders, may result.

Anxiety may lead to hostility, which often is manifested aggressively as wholesome competitiveness, righteous wrath, or outbursts of anger. When hostility is repressed, however, the result is an irreconcilable conflict between desire for power and achievement and desire for affection and admiration. Horney [5] believes the conflict so established is the chief cause of the neuroses. Repressed hostility is the most frequently encountered trait in patients with disseminated neurodermatitis.[6]

Hostility, in turn, often results in feelings of guilt. The person experiencing guilt feels he cannot achieve the goals others or his own conscience have established for him. The result may be an attitude of self-sacrifice, creating tensions that overflow into the autonomic nervous system. Guilt may, on the other hand, dictate the need for self-punishment, with consequent excoriation and mutilation of the skin.

It is an unfortunate paradox that accepted social virtues, such as meticulousness, a ready sense of guilt, and restraint from manifestations of hostility and aggression, are often the cause of psychosomatic disease. It would seem that to be civilized, to be mannerly, to be conscientious, and to be ambitious, is to expose oneself to the danger of neuroses.

PHYSIOLOGICAL FACTORS IN EMOTIONS AND DERMATOSES

The emotions may cause changes in the skin by releasing certain substances at the autonomic nerve endings. These substances, in turn, may act synergistically with other biological factors to cause alterations in the skin. An understanding of these links between emotions and physical agents should reconcile the disputes between the organic and functional schools of etiology.

Two divisions of the autonomic nervous system are recognized: the sympathetic and the parasympathetic. Both divisions have physiological connections with the higher brain centers and may, therefore, be stimulated or inhibited by psychic changes. Parasympathetic fibers in general and sympathetic fibers to sweat glands liberate acetylcholine at their terminals.[7] Acetylcholine causes vasodilatation and secretory activity of the oil glands and sweat glands, (which are, however, of sympathetic innervation). Excitement, hostility, and embarrassment may stimulate these fibers, with subsequent flushing of the skin, oil secretion, and sensations of itching. Release of more acetylcholine causes further permeability of the blood vessels, whereupon whealing, or hives, may occur; still further permeability results in the escape of formed elements of the blood, with consequent purpura and even frank bleeding. Sympathetic fibers (except those to the sweat glands) liberate an epinephrine-like substance called sympathin.[7] Stimulation of this system is seen in reactions to fear and anxiety. Changes in the skin are pallor, coldness, sweating, cutis anserina, and crawling sensations. Some emotions produce a mixture of sympathetic and parasympathetic effects on the skin.

A neurotic person or a normal one under stress tends to have a set pattern of skin response to emotional stimuli. This pattern, if repeated often enough, may cause functional changes to advance to organic disease.[7]

There is a special relationship between allergy and the nervous system. This is explained biologically in the synergism of acetylcholine and histamine. A histamine-like substance is produced at the site of most allergic reactions. Reinforcement by release of acetylcholine of emotional origin at that site may cause histamine to produce a clinical allergic reaction when the concentration of histamine alone would be insufficient to do so.[8] This explains why so many persons experience allergic reactions only when they are emotionally disturbed.

Another important contribution to our knowledge of the interaction between emotional and physical factors is the recent concept of "internal sweating." When the sweat ducts become plugged and sweat continues to be secreted, the pressure within the ducts may rise to 240 mm. Hg.[9] There are over 2 million sweat glands in the human skin. In areas where the glands are occluded by scales or inflammation, it is understandable that retained sweat feels like the pricking and stinging of countless hypodermic injections. Since sweating may be caused by emotional stress, the already inflamed skin rapidly responds to "internal sweating" by a flare-up. These outbursts can sometimes be forestalled by the use of anticholinergic drugs, such as methantheline (Banthine) bromide and diphenmethanil (Prantal) methylsulfate, which inhibit sweating. With sweat retention there may also be retention of allergens that would normally be excreted with the sweat.[9] These allergens, dammed back and under greatly increased pressure, may cause allergic reactions that occur only if sweat is secreted and the sweat ducts are plugged.

ROLE OF EMOTIONS IN SPECIFIC DISEASES

Emotional factors affect two skin diseases of proved organic etiology: warts (verrucae) and fever blisters. The common wart is a benign tumor caused by tissue response to a virus infection. The power of suggestion in curing warts has been known for centuries. Witch doctors and medicine men often gained their reputations by the successful employment of necromancy in treating warts. Mark Twain's Tom Sawyer and Huckleberry Finn effected cures by resorting to nocturnal sorcery. It is ethical practice today to use suggestion in treating warts.

Recurrent herpes simplex as manifested by fever blisters or "cold sores" is another disease of proved virus etiology. The latent virus, carried by most adults, is usually activated by upper respiratory tract infections, fever, upset stomach, and other identifiable factors. A group of 10 patients with recurrent herpes simplex that had no such correlation to organic factors was studied

by Blank and Brody.[10] Nine of the ten patients showed an amazing uniformity in psychological patterns in that they were immature, passive, dependent, and highly suggestible. Hostility was recognized in conflict with their desire to please. Brief psychiatric treatment was usually sufficient to control the attacks of herpes simplex, at least during the period of active psychotherapy. Many patients with recurrent herpes simplex recognize the relationship between emotional disturbances and attacks of this disease.

Blushing, or flushing, is the commonest external manifestation of parasympathetic stimulation. English [3] states that the blush symbolizes inner excitement. A desire to conceal this excitement and fear of its exposure provide psychic stimuli resulting in the blush. Seitz [11] states that blushing is a reaction to guilt and that a consequence of blushing is pruritus and scratching. Common skin disorders such as rosacea, urticaria of psychogenic origin, eczema of the flush areas, solar dermatitis, and lupus erythematosus occur when persons with the flush mechanism are subjected to certain organic disturbances.

Rosacea occurs in persons with the blush tendency who are also subject to gastrointestinal disturbances and menopausal disorders.[12] These patients are quiet, reserved, serious-minded, and bashful.[13] They rarely react aggressively to attack but, rather, become obstinate and sullen. A high level of self-esteem causes them to suppress feelings of guilt and shame. Treatment of rosacea requires that this personality pattern be corrected, as well as the gastrointestinal disorder and the skin blemishes.

Another consequence of the blush mechanism is seen in patients with urticaria of psychogenic origin. An emotional factor is present in most cases of urticaria.[14] Clinical and psychoanalytic studies performed on patients in whom biological causes of urticaria have been satisfactorily excluded delineate personality types that have certain common characteristics.[15] All seem to have intense longings for achievement; they are driving, keyed-up persons, intent on a goal. They often consider themselves wronged or injured, usually by someone in a fairly close family relationship, and regard the situation as one that precludes any personal action.[16] A conflict between the desire for power and the desire for approval results in the vasomotor components of urticarias. Reference has been made to synergism between histamine produced on an allergic basis and acetylcholine produced on an emotional one. This explains the frequent observations that a person can eat tomatoes with no resultant hives except at times when he is emotionally disturbed. Since tension in hard-driving people who long for achievement can usually be lowered by psychotherapy, this method is an important aid in the management of urticaria with psychogenic elements.

Atopic eczema of infancy and childhood is a challenge to several specialties. Many afflicted children carry hereditary allergies, and this factor must be considered in treatment. Carefully directed topical therapy often alleviates the symptoms. A psychiatric approach to the parent has recently afforded a further means of managing this disease. Williams [17] studied atopic dermatitis in children from the standpoint of the maternal rejection factor. Of 33 children examined, 31 manifested symptoms of maternal rejection according to accepted criteria.[18] In the other two cases the mothers demonstrated attitudes suggesting rejection of the child. Therapy was directed mainly toward correction of the mother's behavior toward the child. Favorable results in this series exceeded those achieved by topical applications and conventional methods of therapy in allergy. In childhood eczema there is a constant "battle of the wits" between child and parent, in the course of which the child discovers that his most potent weapon is an orgy of scratching. This weapon is used in retaliation against persons and situations that threaten his sense of security. I have noted the prevalence of eczema in adopted children. While consciously "wanted" by their parents, they sense the presence of unconscious rejection by the mother, to whom the adopted child is, at best, a substitute for the one she could not conceive and whose imagined qualities the foster child fails to fulfill. A psychiatric approach to parents in the therapy of infantile atopic eczema must be accepted as an aid to conventional methods of treatment.

Adult patients with neurodermatitis, or atopic eczema, have certain traits in common with those exhibited by children with eczema. There is a significant frequency of personal and family atopy. Almost invariably anxiety exists, expressed as hostility. This may still have as its target the mother or a mother figure.[19] Unlike the eczematous child, however, the adult with eczema suppresses resentments and turns them inward. This trait has been demonstrated by clinical studies,[6] Rorschach patterns,[20] and the use of other projective tests.[21] Resentment may be disguised as superficial compliance; therefore the patient may appear to be complaisant and acquiescent up to the very moment when he rejects his physician in favor of another therapist. The hostility, on the other hand, may be more overt. In such cases the physician dreads each visit of the patient, with his scepticism toward every proposed remedy. The person with neurodermatitis is very meticulous in his habits. He may produce at each office visit an itemized list of questions to ask the physician. The patient is usually above average in intelligence and is aware that his ambitions surpass his talents. Frustration is the inevitable consequence. He has, literally at his fingernails, a means of emancipation from situations that threaten his adequacy: he scratches.

Most patients with disseminated neurodermatitis benefit from judicious psychotherapy. The ideal therapist would combine the talents of a competent dermatologist, an alert allergist, and a prudent psychiatrist. Combined medical and psychological therapy by one physician is most frequently indicated in cutaneous conditions with emotional aspects.[22] Haphazard psychological probing in the presence of severe or long-standing neuroses, however, is dangerous. It may result in the breaking up of homes, suicide attempts, development of frank perversions, or acute psychotic reactions. These possibilities should be anticipated, and the patient with deep-seated neuroses should be referred for skilled psychiatric treatment. If such care is unavailable, the physician should do the best he can with medical treatment alone.

Seitz and Gorman [23] assert that the dermatologist can practice psychotherapy if he possesses certain qualifica-

tions. He must enjoy helping people, be able to sit quietly and listen comfortably, refrain from displaying restlessness, and possess some training in dynamic psychotherapy. The patient must be one whose skin disorder is not too long-standing; his past history should be one of relatively good adjustment; and his emotional conflicts should be of recent origin. Therapy may safely include supportive methods that reinforce the patient's feelings of adequacy and security, promote harmony, and provide him opportunity to discuss his conflicts.

Localized neurodermatitis, or lichen simplex chronicus, usually appears as isolated patches of thickened skin, with intense itching. Severe scratching or overtreatment may produce acute flare-ups with edema and exudation. Common sites of involvement are the nape of the neck, the pretibial areas, the scrotum, the vulva, and the anal region. Careful search for organic causes must be made before the diagnosis of essential pruritus or neurodermatitis of the anogenital areas becomes tenable. Frequently an organic factor of chemical, mechanical, infectious, or allergic nature starts the process, though it may continue as a purely psychogenic itch, with lichenification or thickening a result of scratching. In either event, the scratch habit becomes so inveterate that if topical and physical agents prove incapable of breaking this vicious cycle of itching, scratching, and lichenification, then psychotherapy must be used. Localized neurodermatitis, while usually not a serious malady, may be the somatic expression of deep-seated emotional disturbance. It may symbolize an erotic substitute for lack of love or an immature means of securing genital pleasure; or the scratching may emanate from a sense of guilt and a consequent need for self-punishment in the form of excoriation. The personality type of these patients does not lend itself to superficial psychological exploration; if psychotherapy is necessary, it should be conducted by one well trained in its methods.

Eczema of the hands is a complex, often disabling disease of diverse etiology. Since the palmar surfaces are especially prone to exhibit emotional sweating, this factor is important in all types of hand eczemas, whether of psychogenic, organic, or allergic etiology. Maceration of the skin by sweat renders it more pervious to chemical irritants and contact allergens. More important is the sweat-retention factor previously mentioned, in which plugging of the sweat ducts occurs with subsequent "internal sweating." This may be the primary cause of dyshidrotic eruptions, and may secondarily intensify hand eczemas of all types.

Frequent references have been made to the role of the emotions in other dermatoses, such as psoriasis,[24] seborrheic dermatitis,[25] lichen planus, alopecia areata,[26] and dermatitis herpetiformis and to the psychological consequences of disfiguring skin diseases such as acne vulgaris and lupus erythematosus.[27]

A few diseases of purely functional nature are encountered by the dermatologist. Delusion of parasitosis [28] is a manifestation of a deep-seated psychosis. In the course of this disease the patient brings rolled-up bits of tissues and crusts he has removed from his skin, asking the physician to identify these "worms" or "bugs" that are crawling on or in him. Phobias commonly encountered by the dermatologist are fear of syphilis and fear of cancer. Klauder [29] believes that burning tongue, for instance, is invariably the expression of fear of cancer, often aroused by indiscreet remarks of a physician. Neurotic excoriations and self-inflicted mutilations, whether imposed upon or independent of coexisting skin disease, may result from guilt feelings and a strong need to disfigure or to cause pain and call attention to oneself in some perverse way; or it may be a conscious means of malingering to secure sympathy or compensation. These functional diseases represent psychiatric problems and are amongst the most severe and intractable psychiatric conditions.

SUMMARY

Commonly encountered emotions such as insecurity, anxiety, hostility, and guilt may cause stimulation of the autonomic nervous system, leading to flushing, sweating, itching, and excoriating. Physical agents through which emotions mediate these effects are acetylcholine released at parasympathetic nerve fiber endings; sympathin produced by sympathetic stimulation; synergism between acetylcholine and histamine; and the mechanical and allergic effects of sweat retained under pressure.

Several skin disorders believed to be of emotional origin exhibit fairly characteristic personality patterns. An effort has been made to relate the clinical entity to the emotional pattern in herpes simplex, rosacea, urticaria, childhood eczema, adult neurodermatitis, and localized neurodermatitis. In most such cases it is desirable that one physician supervise both the somatic and psychic aspects of therapy. Functional dermatoses such as delutions of parasitosis, syphilophobia, dermatitis factitia and neurotic excoriations result from deep-seated neuroses or psychoses and should be referred to the psychiatrist for treatment.

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The Work of a Ship Surgeon.—People are always liable to sudden illness. Cases of acute appendicitis occur now and then in . . . places ideal from a health point of view. The same holds good in the case of ships, however modern and hygienic; indeed, even more so, considering the sudden changes of climate to which all on board are subject during a voyage of any duration, also the dietetic risks taken ashore at various ports of call. To this must be added: (1) the almost invariable presence on board, among the passengers, of cases of chronic illness, e. g., diabetes mellitus, gout, arthritis; (2) the presence on board of the crew, who are "super-liable" to accidents, right round the clock. Passengers seem strangely oblivious of the latter; they mostly have the idea that the doctor is on board primarily in their interests, whereas, . . . in strict legality, there is no onus on the shipowner to provide a surgeon for passengers per se—except in respect of an old-standing legal requirement whereby a doctor has to be provided when 50 or more emigrant or third-class passengers are on board. . . . There is a vast difference between the small "passenger-cargo" ship with just over 100 "souls on board" and the large modern passenger liner. The two Cunarder "Queens" have each, when full, a total complement of round about 5,000 persons on board, to meet the medical needs of whom two surgeons, three nursing sisters, and six hospital or surgery attendants are required. . . . In these large ships, with their relatively huge complements, any sort of emergency may arise at any hour, from which it follows that the surgeons on board have to be "universal" specialists, of a sort able to give at least first aid in the various specialties.—J. S. Meighan, M.D., The Ship-Surgeon's Life, *Practitioner*, May, 1953.

SERUM HEPATITIS FROM POOLED IRRADIATED DRIED PLASMA

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An understanding of the relationship between the occurrence of homologous serum hepatitis and the transfusion of pooled dried human plasma irradiated with ultraviolet light is necessary in order to evaluate the usefulness of the large volume of dried plasma now being manufactured. Early reports [1] indicated that the etiological agent of homologous serum hepatitis is destroyed by ultraviolet irradiation. More recent reports [2] have indicated that the methods of irradiation are not always adequate. The present study was conducted to determine further the role of irradiated dried plasma in the transmission of homologous serum hepatitis.

The plasma used in this study consisted of official test samples submitted by seven licensed processors to the Laboratory of Biologics Control of the National Microbiological Institute for evaluation before release of the material. Samples from each processor are tested for sterility, freedom from pyrogens, hemoglobin content, and solubility and must meet minimum requirements before release for human transfusion. All of the samples used represented lots of plasma manufactured for the armed forces. A record is kept in the Laboratory of Biologics Control of the clinical use of many of these lots of plasma, making possible the patient follow-ups reported here. Patients who received plasma prepared by these seven processors between Jan. 1, 1951, and April 1, 1952, are included. Clinical use was reported by a responsible physician in each of seven hospitals.

The records of 464 patients were investigated, and, of these, 180 could be followed up well enough to be included in the study. The other 284 patients investigated were excluded from the series for the main reasons of: early death (176), incomplete or missing hospital records (35), and inability to locate the patient (69). Since pooled plasma does not have to be typed and is readily available, it was used to treat patients in critical condition, as the result of either chronic disease or acute injury. Early death from these causes accounted for the majority of exclusions. The patients included had received the plasma at least 150 days prior to follow-up examination. No effort was made to determine whether or not human blood products other than plasma and whole blood were used. When possible, patients were interviewed in order to determine the presence of serum hepatitis. They were not asked leading questions, but were encouraged to relate their symptoms if any had occurred. They were questioned about general health, specific diseases, ability to work, contacts, malaise, anorexia, nausea and vomiting, abdominal tenderness, and pruritus, as well as jaundice. A patient who could not be interviewed because he had left the locality or had died was included in the series only if he had been examined by a physician at least once every two months from the second to the sixth month after receiving the plasma. Contact with private patients was made by the attending physician, and the information was accepted in writing.

The 180 patients in this study received a total of 403 units of plasma containing 600 cc. each. Sixty-four patients (35.5%) received plasma alone, while the rest (64.5%) received whole blood as well. Twenty-three patients, or 12.8% of the 180, had a history of signs and symptoms of serum hepatitis. Of the 64 patients who received only plasma, 6 (9.3%) later had hepatitis. No patients were included who did not show jaundice. Two additional cases of jaundice were found in which a history of exposure to infectious hepatitis eliminated the diagnosis of definite serum hepatitis. Two other cases of jaundice were considered to be secondary to biliary obstruction. Twenty of the 23 cases were diagnosed on readmission of the patients to the hospital, and the other 3 were diagnosed from the history given on personal interview. Table 1 shows the number of patients studied at each hospital and the incidence of hepatitis found.

TABLE 1.—*Incidence of Serum Hepatitis Among Patients Receiving Irradiated Plasma*

Hospital	No. of Patients Studied	Cases of Hepatitis	Incidence of Hepatitis, %	Deaths
1	33	2	6.0	1
2	27	2	7.4	..
3 *	..	..	...	..
4	17	5	29.4	2
5	60	8	13.3	2
6	30	3	10.0	1
7	13	3	23.0	1
Total	180	23	12.8	7

* In hospital 3, the 12 patients who received the plasma were not available for the study.

In the 23 cases of hepatitis presumably resulting from the administration of whole blood or irradiated plasma, there were 7 (30.5%) deaths apparently due to hepatitis. There was one other death among the persons who contracted the disease, but this was probably a direct result of the primary disease, with the hepatitis as a contributing factor. Plasma from each of the seven processors was involved in one or more cases of hepatitis. Table 2 shows the manufacturers and amounts of plasma given in the 23 cases of hepatitis. Dried plasma prepared from fresh

From the Laboratory of Biologics Control, National Microbiological Institute, National Institutes of Health.

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2. Rosenthal, N.; Bassen, F. A., and Michael, S. R.: Probable Transmission of Viral Hepatitis by Ultraviolet-Irradiated Plasma: Report of 3 Cases, J. A. M. A. **144**: 224-226 (Sept. 16) 1950. Greenlee, R. G.; Terrill, R. J., and Sloan, J. Q.: Homologous Serum Hepatitis After Transfusions of Blood and Ultraviolet-Irradiated Plasma, Texas State J. Med. **47**: 831-835, 1951.

blood as well as reprocessed * plasma was involved, and there was no apparent relation between the number of cases and type of plasma, nor was a relation found between the number of cases of hepatitis and the method of ultraviolet irradiation.

COMMENT

The attack rate of serum hepatitis resulting from the injection of infected material is estimated by Paine and Janeway [3] as being about 40%. This incidence agrees with that obtained by Murray and others [4] in experimentally induced hepatitis. The fact that the present study shows a lower rate (12.8%) is probably the result of several factors. Perhaps most important is the indication that ultraviolet irradiation is effective to some degree, although not completely. Furthermore, in view of the fact that other studies of this disease [5] have revealed a definite incidence of nonicteric cases of serum hepatitis, it seems likely that there were additional undiagnosed cases and that the true incidence of the disease was higher than reported here. Studies showing an incidence of nonicteric hepatitis have, however, been those in which laboratory studies were possible, which was not the case in this series.

Many patients receiving plasma also receive whole blood, and nearly all receive many skin punctures by instruments that may be ineffectively sterilized. Since reports indicate that as little as 0.0001 to 0.00001 cc. of infected material can transmit the disease,[6] the origin of the infection may often remain questionable. Although a skin test for infectious hepatitis has been described,[7] it was not utilized in this study. Since only a positive history of contact combined with short incubation distinguishes infectious hepatitis from serum hepatitis, this similar disease serves to confuse the issue further. A study to determine the occurrence of serum hepatitis can be absolute only in a negative way; that is, if no cases of serum hepatitis can be elicited in a significant number of patients, then the plasma has not been infective. On the other hand, evidence of cases occurring may be of value if the total incidence is significantly higher than the incidence of endemic infectious hepatitis and whole blood transfusion hepatitis.

TABLE 2.—*Cases of Serum Hepatitis*

Patient No.	Sex	Race	Age	Plasma Processor (Units of Plasma)							Total Units of Plasma		Whole Blood, Total Units	Incubation Period, Days	Deaths
				A	B	C	D	E	F	G	Fresh	Reprocessed			
1	M	W	49	12	..	10	..	1	..	..	13	10	7	211	..
2	M	W	22	3	..	2	..	..	..	..	3	2	26	50	..
3	M	W	35	..	..	1	..	..	..	..	..	1	2	80	X
4	M	W	78	..	..	1	..	..	..	..	..	1	1	112	..
5	M	W	40	..	..	1	..	..	..	..	..	1	2	149	..
6	M	N	32	..	5	..	..	..	2	..	2	5	14	98	X
7	F	N	30	..	..	1	..	..	..	..	..	1	..	62	..
8	M	W	50	..	..	..	..	..	1	..	..	1	..	46	..
9	F	W	27	..	..	1	..	..	..	..	..	1	3	181	..
10	M	W	56	..	..	21	..	..	..	..	..	21	3±	84	X
11	F	W	43	..	..	1	..	..	..	..	1	..	2±	87	..
12	F	W	39	1	..	..	..	..	..	..	1	..	..	67	..
13	M	N	42	..	..	..	..	..	..	2	2	..	..	130	..
14	M	N	72	1	..	..	..	..	..	..	1	..	10	93	..
15	M	W	46	3	..	..	..	2	1	..	6	..	4	94	..
16	M	W	56	1	..	1	..	..	1	..	3	..	5	78	X
17	M	N	66	1	..	..	..	..	..	..	1	..	..	62	X
18	F	W	51	..	..	1	..	..	..	..	..	1	..	112	..
19	M	W	60	..	..	1	..	..	1	..	1	1	3	120	..
20	M	W	29	..	..	..	1	..	..	..	..	1	16	62	..
21	M	N	40	1	..	..	1	..	..	..	2	..	1	57	X
22	F	W	70	1	..	..	..	..	..	..	1	..	1	68	X
23	F	N	50	1	..	..	..	..	..	..	1	..	4	78	..

The occurrence of serum hepatitis as the result of the transfusion of whole blood is generally considered to be less than 0.5%.[8] The incidence of infectious hepatitis in one of the three cities in which this study was done was 0.02% per year; 198 cases were reported in 1951 in a population of 985,000. Of the 77 patients who had received plasma (and in some instances whole blood as well) in this city, 13 (16.7%) later had jaundice. The percentage of jaundice found in this group of patients is then far higher than the probable combined occurrence of infectious hepatitis and hepatitis from blood transfusions.

The seven deaths were about evenly distributed among patients in the fourth to eighth decades of life (fig. 1). In the third decade, which is well represented, no deaths occurred. Although the number was too small to be significant, the mortality rate was compatible with other reported studies.[9]

The findings in this study indicate that ultraviolet irradiation of pooled plasma by method of large-scale

* Reprocessed plasma is that which has been processed to the final stage once and is then reconstituted, pooled, clarified, irradiated, dispensed into the final container, dried, and finally tested. The reprocessed plasma referred to here had not been irradiated during the original processing, and was, therefore, reprocessed in order to expose it to ultraviolet irradiation.

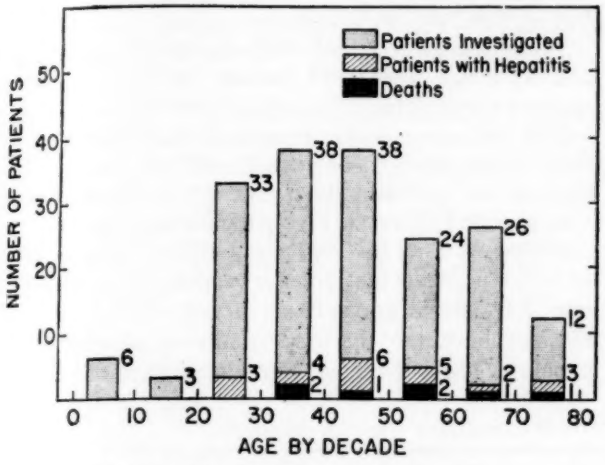
3. Paine, R. S., and Janeway, C. A.: Human Albumin Infusions and Homologous Serum Jaundice, J. A. M. A. **150**: 199-202 (Sept. 20) 1952.

4. Murray, R.; Diefenbach, W. C. L.; Ratner, F., and Leone, N. C.: Effect of Heat on the Agent of Homologous Serum Hepatitis, Laboratory of Biologics Control, National Microbiological Institute, National Institutes of Health, Bethesda, Md., to be published.

5. Memorandum prepared by Medical Officers of the Ministry of Health: Homologous Serum Jaundice, Lancet **1**: 83-88, 1943. Barker, M. H.; Capps, R. B., and Allen, F. W.: Acute Infectious Hepatitis in the Mediterranean Theater, Including Acute Hepatitis Without Jaundice, J. A. M. A. **128**: 997-1003 (Aug. 4) 1945. Scheinberg, I. H.; Kinney, T. D., and Janeway, C. A.: Homologous Serum Jaundice: A Problem in the Operation of Blood Banks, J. A. M. A. **134**: 841-848 (July 5) 1947.

6. Drake, M. E., and others: Effect of Nitrogen Mustard on Virus of Serum Hepatitis in Whole Blood, Proc. Soc. Exper. Biol. & Med. **80**: 310-313, 1952. Paine and Janeway.[3] Murray and others.[4]

production is not wholly effective for complete destruction of the agent of homologous serum hepatitis. Transfusion of pooled dried plasma, even though irradiated,


Patients Investigated
Patients with Hepatitis
Deaths
NUMBER OF PATIENTS
AGE BY DECADE
0 10 20 30 40 50 60 70 80
10 20 30 40 50
6 3 33 3 38 4 2 38 6 1 24 5 2 26 2 12 3

Incidence of hepatitis and deaths by age groups.

involves a calculated risk that should be considered carefully in relation to the need of the patient for this therapeutic agent.

SUMMARY AND CONCLUSIONS

Four hundred and sixty-four records of patients who had received pooled. dried irradiated human plasma 150 or more days previously were investigated. The records of 180 patients were found adequate to warrant a study of the occurrence of serum hepatitis as a result of the plasma transfusion. Twenty-three or 12.8% of the 180 patients had signs and symptoms of serum hepatitis. Seven or 30.5% had died as a direct result of the disease or a combination of their original disease and the hepatitis. Of 64 patients who had received only plasma and no whole blood, 6 (9.3%) had hepatitis. The occurrence of a 12.8% incidence of hepatitis is considered significantly higher than that of hepatitis as the result of blood transfusion alone (0.5%) or the incidence of infectious hepatitis (0.02%). The findings indicate that the methods now used for the irradiation of pooled plasma in large-scale production are not wholly effective in complete destruction of the agent of homologous serum hepatitis.

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SERUM HEPATITIS APPARENTLY ACQUIRED FROM IRRADIATED PLASMA

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Pooled human plasma, untreated, has been a frequent cause of serum hepatitis. Blood from one donor carrying the virus can make a whole pool infectious. Obviously the likelihood of plasma being infected varies with the number of donors making up the pool. Plasma from a large pool is more frequently infected than plasma from a small pool. The probability of contracting serum hepatitis from a whole blood transfusion is extremely small. Paine and Janeway [1] have analyzed reports on this subject.

Exposing plasma to ultraviolet light seemed to obviate this hazard. Known icterogenic serum so treated has been given in small quantities to volunteers without causing hepatitis.[2] MacCallum,[3] on the other hand, used a different technique of irradiation that failed to prevent the transmission of hepatitis. Irradiation of plasma has been required by the National Institutes of Health since April, 1949, as a prerequisite to licensing manufacturers.

That irradiation does not always inactivate the virus was shown by James, Korns, and Wright [4] who reported the occurrence of 12 cases of serum hepatitis among 20 recipients of one lot of irradiated plasma. Of course this outbreak could have been due to faulty irradiation of the plasma involved, rather than to the inefficacy of irradiation as a means of inactivating hepatitis virus. There have been other reports [5] attributing serum hepatitis to irradiated plasma, but this apparent association could have been coincidental rather than causal. To pursue this problem further, a series of patients who received irradiated plasma from several sources was studied to determine whether irradiated plasma, as it is routinely prepared for commercial distribution, carries with it a definite risk of producing serum hepatitis.

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MATERIALS AND METHODS

All patients receiving irradiated plasma during the period from late 1949 to early 1952 in three upstate New York hospitals were studied. The hospitals were chosen because they had accurate and generally complete records of the lot numbers of the plasma used. Two of the hospitals obtained their plasma from a single commercial source (plasma B), and the third used plasma from the same as well as another commercial source (plasma A). The pools ranged in size from 51 to 256 donors, averaging 114, for plasma B and from 53 to 178 donors, averaging 150 for plasma A. The plasma was processed in accordance with the requirements of the National Institutes of Health. Since many of the patients received whole blood in addition and since nearly all hospitalized patients received some sort of needle injection during their stay, it was necessary to evaluate these possible sources of infection. Furthermore, subsequent jaundice in these patients might have been due to naturally acquired infectious hepatitis. In order to assess these factors, a control group was studied. Controls for the recipients of plasma plus whole blood were chosen from the hospital blood bank list of whole blood recipients. Controls for the plasma recipients who did not receive whole blood were chosen from a list of hospital admissions. These persons were selected without prior knowledge of the outcome of their illness. The first patient listed who was of the same sex and roughly the same age as the plasma recipient and who was a patient in the hospital at the same time was chosen as the matched control. Most of each group were surgical patients. None of those in whom hepatitis later developed had been given human thrombin, a reported source of serum hepatitis.[6]

Many plasma recipients died shortly after transfusion and were not considered further. Of the 149 plasma recipients remaining for study, 11 were lost from observation, one was excluded because he had hepatitis at the time of the plasma transfusion, and one was excluded because she had been given a variety of blood products over a period of years. Five patients were excluded because they did not survive the possible incubation period of serum hepatitis that, for the purpose of the investigation, was defined as one to six months and because they did not have the full opportunity to acquire serum hepatitis. These five died, without evidence of hepatitis, at intervals ranging from two to five months after the plasma transfusion; thus, 131 plasma recipients were included in the study group. The control group was restricted, in the same way, to those who survived the six month period following the last plasma transfusion given to the matched plasma recipient. If a control died from a cause other than hepatitis during this six month period, another was selected to replace him; thus, the control group consisted of 131 patients.

Efforts to detect hepatitis in these groups consisted of a review of the hospital records, a letter of inquiry to the attending physician, and a visit by the epidemiologist to the patient. Six of the 131 in the study group, and six of the 131 controls had died by the time the study was initiated, although they had all lived at least six months after the last plasma transfusion. In these instances, their families were interviewed. The purpose of the visit was to ascertain whether the plasma recipient, or the control, had suffered from hepatitis or an illness suggestive of hepatitis that was unknown to the hospital or to the physician in attendance at the time of hospitalization. Home visits were made to both groups of patients from

TABLE 1.—*Pertinent Data on Eleven Patients in Whom Serum Hepatitis Developed*

Case	Hospital	Age, Yr.	Sex	Dates of Transfusions of Blood and Plasma	Number and Type of Transfusions: Whole Blood, Units	Plasma: Code No.*	Plasma: Units	Condition for Which Transfusion Was Given	Date of Onset of Jaundice	Incubation Period, Days
1	A	47	M	9/16/49	3	B1	1	Bleeding duodenal ulcer	1/11/50	117
						B2	1			
						B3	1			
2	A	65	M	11/ 2/49	0	B4	1	Resection of prostate	1/27/50	86
						B5	1			
3	A	78	M	11/30/49	1	A1	1	Auto accident	2/27/50	89
						B6	1			
4	A	52	F	5/ 5/50	3	A1	1	Cancer of urethra	7/13/50	69
						A2	1			
5	A	36	M	5/ 9/50	1	A3	1	Tonsillectomy	About 7/26/50	About 78
6	A	32	M	5/17 and 5/23/50	0	A1	1	Psoriasis and pemphigus	8/14/50	83 or 89
						A3	1			
7	A	50	M	7/20/50	0	A2	2	Bleeding gastric ulcer	10/ 1/50	73
8	C	73	F	8/ 9/51 to 8/11/51	3	B7	2	Cholecystitis and cholecystectomy	About 11/11/50	About 92 to 94
9	C	43	M	10/15/51 to 10/20/51	4	0	0	Ruptured urethra due to trauma	1/ 5/52	77 to 82
10	C	42	M	12/27/51	0	B8	1	Burns	3/28/52	92
11	C	24	M	12/27/51 to 2/ 1/52	16	B8	3	Burns	2/26/52	25 to 61
						B9	2			
						B10	3			
						B11	8			
						B12	4			

* Plasma is designated A or B, depending on the commercial source; arabic numerals represent different lots of plasma.

5. Rosenthal, N.; Bassen, F. A., and Michael, S. R.: Probable Transmission of Viral Hepatitis by Ultraviolet Irradiated Plasma, J. A. M. A. **144**: 224-226 (Sept. 16) 1950. Barnett, R. N.; Fox, R. A., and Snavely, J. G.: Hepatitis Following the Use of Irradiated Human Plasma, ibid. **144**: 226-228 (Sept. 16) 1950. Greenlee, R. G.; Terrill, R. J., and Sloan, J. Q.: Homologous Serum Hepatitis After Transfusions of Blood and Ultraviolet-Irradiated Plasma, Texas State J. Med. **47**: 831-835 (Dec.) 1951. Thompson, J. L., Jr., and Sutliff, W. D.: Viral Hepatitis Following the Use of Ultraviolet Irradiated Human Plasma, South. M. J. **45**: 801-805 (Sept.) 1952. Unpublished data on file, New York State Department of Health.

6. Lesses, M. F., and Hamolsky, M. W.: Epidemic of Homologous Serum Hepatitis Apparently Caused by Human Thrombin, J. A. M. A. **147**: 727-730 (Oct. 20) 1951.

hospitals A and B, but, since hitherto unknown cases of hepatitis with icterus or instances of illness suggestive of hepatitis without icterus were not revealed, the visits were omitted in the study of the groups from hospital C. Investigation of study and control groups was carried out with equal thoroughness.

TABLE 2.—*Cases of Hepatitis, According to Hospital and Type of Blood Product Given, Occurring One to Six Months After Transfusion*

Hospital	A		B		C		Total	
Group	Recipients	Cases	Recipients	Cases	Recipients	Cases	Recipients	Cases
Plasma only	17	3	10	0	13	1	40	4
Plasma and whole blood	50	4	10	0	31	2	91	6
Whole blood	49	0	10	0	32	1	91	1
No blood	18	0	10	0	12	0	40	0
Total	134	7	40	0	88	4	262	11

Overt jaundice was chosen by definition as an essential criterion of hepatitis because the diagnosis of hepatitis without icterus, if not made at the time of illness, could hardly be established later.

RESULTS

In the 131 recipients of plasma studied, hepatitis, as defined above, developed in 10, or 7.6%. In contrast, in the 131 controls, hepatitis developed in only one, or 0.8%. All cases of hepatitis had been previously recognized as such by the attending physician. Review of the clinical and laboratory details by the epidemiologist served to confirm the impression that the illnesses were typical of icteric infectious or serum hepatitis. None of the patients had a previous history of hepatitis. None had a history of biliary disease except one (case 8, table 1). No blood donor gave blood to more than one of these persons with hepatitis. Other pertinent details are listed in table 1. There were no deaths caused by hepatitis. The incubation period ranged from 69 to 117 days except in one instance (case 11, table 1) in which it could have been any interval from 25 to 61 days. The day when jaundice was first noted was considered the day of onset.

Hepatitis occurred in patients from hospitals A and C but not from hospital B (table 2); however, this may be explained by the small number of recipients included in the study from hospital B. Six of the 10 hepatitis cases were among 91 patients who received plasma plus whole blood, and the other 4 were among the 40 patients who received plasma only. The control in whom hepatitis developed had received whole blood. Table 3 presents the incidence of hepatitis in patient and control populations by age groups. The absence of hepatitis in the group under 20 years of age may be a chance observation; on the other hand, it is in agreement with the reported experience of others [7] and may be a reflection of relative resistance or of a smaller proportion of icteric disease in this age group.

The 40 patients given plasma but not whole blood each received an average of 1.5 units of plasma. Some of the patients received more than one unit of the same lot. Since minute amounts of plasma can transmit serum hepatitis, multiple units from the same pool of donors may represent little or no greater risk than one unit; on the other hand, it is necessary to consider how many different lots of plasma were received by the average patient. This numbered 1.2.

Each of the 91 patients given plasma and whole blood received an average of 4.5 units of whole blood (totaling 410 units) and 2.4 units of plasma, of which 1.5 were from different lots. The 91 matched controls each received an average of 2.4 units of whole blood (totaling 215 units). Although most of each group were surgical patients, a greater proportion of the controls consisted of patients undergoing elective surgery. This may explain the reason for which they were given less whole blood. This difference in the number of whole blood transfusions does not account for the fact that there were 6 cases of hepatitis among the 91 plasma and blood recipients and only one case in the 91 controls receiving whole blood.

TABLE 3.—*Cases of Hepatitis, According to Patient's Age and Type of Blood Product Given, Occurring One to Six Months After Transfusion*

	Recipients				Cases of Hepatitis				Attack Rate, %	
	Experimental		Controls		Experimental		Controls			
Age, Yr.	Plasma	Plasma and Whole Blood	Whole Blood	No Blood	Plasma	Plasma and Whole Blood	Whole Blood	No Blood	Experimental	Controls
Under 20	8	12	7	10	0	0	0	0	0.0	0.0
20 to 29	7	17	13	6	0	1	0	0	4.2	0.0
30 to 49	11	24	30	13	2	2	1	0	11.4	2.3
50 to 69	9	25	27	9	2	1	0	0	8.8	0.0
70 and over	5	13	14	2	0	2	0	0	11.1	0.0
Total	40	91	91	40	4	6	1	0	7.6	0.8

The reports analyzed by Paine and Janeway [1] indicate that about 0.2% of whole blood transfusions cause hepatitis with jaundice. The highest rate (0.35%) was that found by Lehane and co-workers.[8] Even with this high rate of 0.35% one would expect only 1.4 cases in the 91 plasma and whole blood recipients and 0.8 cases in the 91 matched controls. The true incidence of hepatitis with icterus in recipients of whole blood is probably less than 0.35%. There was no correlation between the number of whole blood transfusions per patient and subsequent development of serum hepatitis (table 4).

7. Brightman, I. J., and Korns, R. F.: Homologous Serum Jaundice in Recipients of Pooled Plasma, J. A. M. A. **135**: 268-272 (Oct. 4) 1947.

8. Lehane, D.; Kwantes, C. M. S.; Upward, M. G., and Thomson, D. R.: Homologous Serum Jaundice, Brit. M. J. **2**: 572-574 (Sept. 10) 1949.

Paine and Janeway [1] estimated, from various reports, the carrier rate of serum hepatitis in the population of blood donors and the percentage of recipients of icterogenic material in whom hepatitis with icterus developed. We did not attempt to use their estimates for the purpose of calculating the number of cases of hepatitis that might have been expected had the plasma not been irradiated.

TABLE 4.—*Whole Blood Transfusions Given to Plasma Recipients and Controls Aged Twenty or Over*

Number of Whole Blood Transfusions	Recipients	Cases of Serum Hepatitis	
		No.	%
0	62	4	6
1	62	2	3
2 to 3	56	3	5
4 or more	45	2	4
Total	225	11	5

There are too many variables, not the least of which is the actual prevalence of carriers in the donor population, to permit reliable conclusions.

It was planned to evaluate the icterogenicity of each lot of plasma; however, of the 56 plasma lots studied, very few had been given to more than a handful of patients. For example, 25 of these lots were given to only one patient each. Nevertheless, table 1 shows that in plasma recipients in whom serum hepatitis developed, a minimum of seven lots were involved (if all 10 cases were acquired through this mechanism). Attempts were made to study the experience elsewhere in the United States with other units of these same seven lots of plasma, but barriers to adequate follow-up prevented further investigation.

It might be suggested that the discovered serum hepatitis was related only to plasma processed early in the experience with this technique and that later improvements in the irradiation procedure allowed the production of virus-free plasma. In reality, however, hepatitis occurred in patients receiving plasma irradiated in 1949, 1950, and 1951 (table 5). The relative icterogenicity of

TABLE 5.—*Cases of Hepatitis Occurring One to Six Months After Transfusion Among Recipients of Irradiated Plasma by Year of Irradiation*

Year of Irradiation	Average Number Different Lots per Recipient	Number of Recipients *	Cases †	
			Number	Attack Rate, %
1949	1.3	56	7	12.5
1950	1.3	56	1	1.8
1951	1.3	18	2	11.1
Unknown	...	8	0	0.0

* Five persons receiving plasma irradiated in 1949 and 1950 and two persons receiving plasma irradiated in 1950 and 1951 were included in both years.

† Of the four cases of hepatitis in patients who received plasma but not whole blood, three occurred in recipients of plasma irradiated in 1949 and one in recipient of plasma irradiated in 1951.

plasma irradiated in different years cannot be properly assessed because of the small numbers of recipients and cases involved.

COMMENT

The purpose of this study was to learn if administration of irradiated plasma, as it is routinely prepared for commercial distribution, carries with it a definite risk of producing serum hepatitis. The tenfold difference, observed in this study, in the attack rates of hepatitis in recipients of irradiated plasma compared with the attack rates in matched controls, suggests strongly that irradiation did little to reduce the risk of serum hepatitis. It seems unlikely that any of the cases observed represented naturally acquired infectious hepatitis, since this disease was not known to be present in the environment of the patients either in or out of the hospital. The scattering of onset dates over a three year period and the observed interval, ranging from 61 to 117 days, between receipt of plasma and onset of jaundice are more suggestive of serum hepatitis. No secondary cases among the family and other contacts developed, as might have been expected had the disease been infectious hepatitis. The fairly close similarity between plasma recipients and matched controls, except for the one item of plasma administration, argues strongly against the possibility that other modes of transmission, such as needles, syringes, or surgical instruments, played a significant role. All three of the hospitals followed the practice of autoclaving syringes and needles after each use. As was stated earlier, human thrombin [6] was not administered to any of the patients in whom serum hepatitis developed.

Obviously the series is too small to allow exact definition of the risk from irradiated plasma, and one may draw conclusions only with regard to the particular lots studied. Since probably at least 9 of 131 plasma recipients acquired serum hepatitis from the plasma and since each had received an average of 1.3 units from different lots, the risk of contracting the disease from a single unit may be calculated as 5%. This estimate does not take into account the 11 recipients who were lost and the 7 who were excluded from the study, although, it indicates an appreciable risk of about 4.5% as described by Brightman and Korns [7] in their study of dried, pooled, unirradiated plasma. Since it is not known how many cases of serum hepatitis would have occurred had the plasma not been irradiated, it is not possible to state categorically that irradiation failed to reduce the icterogenicity of the particular lots studied. These findings raise serious doubts, however, as to the value of this procedure. The question of whether the techniques of irradiation can be or have been improved to uniformly destroy hepatitis virus is not within the province of this report.

SUMMARY AND CONCLUSIONS

One hundred thirty-one recipients of irradiated plasma and 131 matched controls from three hospitals were studied in order to determine the incidence of hepatitis during the period one to six months after plasma administration. Ten cases (7.6%) of acute hepatitis occurred in the group receiving the plasma, and one case (0.8%) occurred among the controls. It is believed that the cases in the group receiving plasma can be attributed to that source and that irradiation of the plasma lots studied failed to prevent or to significantly reduce the transmission of serum hepatitis.

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CLINICAL NOTES

SPONTANEOUS PERFORATION OF SIGMOID COLON IN PRESENCE OF DIVERTICULOSIS

REPORT OF TWO CASES WITHOUT EVIDENCE OF INFLAMED DIVERTICULA

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It is widely recognized that perforation of the sigmoid colon leading to abscess formation or spreading peritonitis is a common complication of sigmoid diverticulitis. Much less common but occasionally reported is free perforation into the peritoneal cavity occurring soon after the onset of symptoms.[1] The two cases reported here differ, however, from any we have been able to find reported in the literature. Not only was perforation not preceded by symptoms or signs of diverticulitis, but at operation no inflamed diverticula were noted, although diverticula containing inspissated feces were palpated on either side of the perforation in both instances. We believe it is important to call attention to the possibility of spontaneous perforation in the presence of diverticulosis. In operating on patients with acute abdominal conditions, the surgeon at times discovers peritonitis without obvious cause. We are convinced from our experience with these two patients that the possibility of perforation of the sigmoid colon should not be dismissed in these instances because of the lack of inflammatory signs in the sigmoid and that a most painstaking examination of the sigmoid may at times be required to locate the perforation. The presence of diverticulosis should alert the surgeon to this possibility.

REPORT OF CASES

CASE 1.—A 65-year-old white man entered the Hospital of the University of Pennsylvania March 8, 1952, because of abdominal pain, which had begun suddenly three hours previously. Prior to this illness he had considered himself in excellent health and had been working as a laborer. Careful questioning elicited no admission of previous symptoms of gastrointestinal disease. The pain for which the patient came to the hospital was generalized and severe, and soon after the onset of pain he began to vomit.

On examination, immediately after admission, the patient was thought to be in shock, as evidenced by pale, cold, sweaty skin, a weak pulse, and a blood pressure of 70/40 mm. Hg. Peristalsis was not audible. The rectal temperature was 103 F. The abdomen was tender throughout, with generalized muscular rigidity and rebound pain. A rectal examination disclosed no abnormalities. The hemoglobin level was 12.5 gm. per 100 cc. (Klett-Summerson photoelectric colorimeter), and the leukocyte count was 19,000 per cubic millimeter. Urinalysis showed no abnormalities.

Whole blood was given intravenously, and within 45 minutes the patient's blood pressure had risen to 125/55 mm. Hg. A diagnosis of a massive mesenteric vascular occlusion was made, and the patient was operated on by one of us (W. T. F.), with general anesthesia administered by means of endotracheal technique, about 90 minutes after admission. The peritoneum was opened by an incision in the lower midline. Feces were noted in the right lower quadrant of the peritoneal cavity, but no perforation was found in the appendix, cecum, or ascending colon. Diverticula containing inspissated feces were palpated in a 6 in. (15.2 cm.) segment of midsigmoid colon, but no signs of inflammation were apparent, and no perforation was readily visualized. This portion of the colon was mobilized by division of the lateral peritoneal reflexion. A careful examination of the area showed a 1½ cm. perforation on the antimesenteric border hidden beneath a normal appearing fat tab. An 8 in. (20.3 cm.) segment of sigmoid colon with the perforation at its center was exteriorized through a left lower quadrant stab wound. The edges of the perforated bowel were sutured about a soft rubber tube.

After the operation the patient was treated with continuous gastric suction drainage, intravenously administered fluids, penicillin, and streptomycin. On the seventh postoperative day the exteriorized segment of sigmoid was excised by electric cautery. The patient was discharged March 23, 1952, with his wounds well healed, his colonic stoma functioning well, and his temperature normal. On April 24, he was readmitted for closure of the stoma. Roentgen examination of the colon prior to closure showed diverticulosis without evidence of diverticulitis. The patient had an uneventful recovery after stoma closure, and, at the time of discharge, May 14, 1952, he was having normal bowel movements. Since that time he has been well.

CASE 2.—A 57-year-old white man entered the Hospital of the University of Pennsylvania Aug. 8, 1952, because of severe abdominal pain of three hours' duration. The pain had begun suddenly during defecation, immediately after the patient had eaten a normal breakfast. The pain radiated from the periumbilical region to both sides of the abdomen. The patient tried to take a sodium chloride solution enema soon after onset of the pain but stopped after administering one cupful because of exaggeration of the pain. The patient had considered himself to be in good health until this illness.

Physical examination after admission to the hospital revealed an acutely ill man with excruciating abdominal pain. The blood pressure was 130/80 mm. Hg, the pulse rate was 80 beats per minute, the respiratory rate was 22, and the rectal temperature was 100 F. Peristaltic sounds were not heard. The entire abdomen was rigid and tender, but the symptoms were severest in the right upper quadrant. No tenderness or masses were noted on rectal examination. The hemoglobin level was 15 gm. per 100 cc., and the leukocyte count was 14,500 per cubic millimeter. Urinalysis showed no abnormalities.

The patient was operated on by one of us (W. T. F.), with general anesthesia administered by means of an endotracheal technique, about one and a half hours after admission. Because the signs were severest in the right upper quadrant, a preoperative diagnosis of perforated duodenal ulcer was made, and the abdomen was opened by a short incision in the right subcostal region. Cloudy fluid was present in the right upper quadrant, but no perforation could be found. Palpation of the lower abdomen through the upper abdominal incision revealed free feces in the peritoneal cavity. An incision in the lower right rectus region was then made. The lower peritoneal cavity contained feces and large, undigested food particles. Several diverticula containing inspissated feces were palpated in the sigmoid colon, but no hyperemia, fibrinous exudate, or other sign of diverticulitis was noted. A careful search of the involved area of sigmoid, after mobilization by division of the lateral peritoneal reflexion, showed a 1 cm. perforation in the midsigmoid on the antimesenteric border. About 8 in. of the involved segment was brought out through a stab wound in the left lower quadrant, and the edges of the perforation were sutured about a soft rubber tube.

Postoperatively, the patient was treated with blood and other intravenously administered fluids, penicillin, streptomycin, and intestinal suction drainage with a Miller-Abbott tube. His postoperative course was good, except for the development of a wound infection in the upper part of the right rectus wound.

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1. Weeks, A., and Brooks, L.: Ruptured Diverticulitis with Generalized Peritonitis, S. Clin. North America **6**: 375-376, 1926. Weeder, S. D.: Perforated Diverticulitis of the Sigmoid, Ann. Surg. **93**: 782-785, 1931. Taylor, V. J. M.: A Case of Perforated Diverticulitis, Brit. M. J. **1**: 1124-1125, 1932. Lazarus, J. A.: Perforated Sigmoiditis with Generalized Peritonitis, Am. J. Surg. **22**: 284-289, 1933.

He was discharged Sept. 12, 1952, afebrile and with the colonic stoma functioning well. His stoma was closed without incident in January, 1953, and he has since been well.

COMMENT

Although diverticula were present in the sigmoid colon in these two patients, no signs of diverticulitis were noted at operation, and no symptoms indicating bowel inflammation had been present before the sudden onset of acute pain, indicating perforation. We do not know the cause of the perforation in either instance, but we believe tightly packed feces in a diverticulum may have produced obstruction and gangrene of the wall of the diverticulum. The perforation was almost certainly sudden in both instances, as indicated by the sudden onset of the symptoms and the absence of signs of a walling-off process at operation. Unless the sigmoid colon had been mobilized and carefully examined in these two instances, the perforation would not have been found. The only sign pointing to the perforation was the presence of surrounding diverticula, which were not inflamed.

SUMMARY

Two cases of spontaneous perforation of the sigmoid colon in the presence of diverticulosis are reported. Neither patient had symptoms or signs of diverticulitis. If a careful search of the sigmoid colon had not been made, we would not have identified the perforation in either instance.

CHLOROQUINE DIPHOSPHATE IN TREATMENT OF DISCOID LUPUS ERYTHEMATOSUS

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Since the initial success of the treatment of lupus erythematosus with quinacrine (Atabrine) by Prokoptchouk [1a] and Popoff and Kutinscheff [1b] and later by Page,[2] in Europe, attempts have been made to find other less toxic antimalarial agents. Numerous investigators [3] in this country also have had good results with the use of quinacrine in this disorder, but they have warned about its toxic effects, which may include production of fatal aplastic anemia.[3b]

After conferences with Dr. Leon Schmidt,[4] director of malarial research at the Institute of Medical Research, Christ Hospital, chloroquine was selected as investigative material, because it is distinctly less toxic, it may be found in the skin in appreciable amounts after oral ingestion, and it does not discolor the skin as does quinacrine. A review of the literature and our own experience revealed that the toxic effects of chloroquine diphosphate are insignificant. Toxic symptoms may include pruritus, nausea, anorexia, diarrhea, headache, difficulty in visual accommodation, and weight loss.[5] Rarely, lichenoid dermatitis may occur.[6] With Dr. Schmidt, we are now making detailed assay studies of the patterns of serum and skin distribution of chloroquine diphosphate.

Patients receiving chloroquine diphosphate for lupus erythematosus have been under observation for six months. The average dose has been 0.25 gm. twice daily for one or two weeks followed by 0.25 gm. daily for four to six weeks. In some patients the initial dose was 0.25 gm. three times daily for one or two weeks. These preliminary studies indicate that chloroquine diphosphate is as effective as quinacrine in the treatment of discoid lupus erythematosus (see the table). In some patients the initial response appeared to be slower than is usually the case with quinacrine. New lesions developed in three patients while they were receiving treatment, although the previous lesions continued to improve. It is important to note that two patients who had severe nausea and emesis as a result of quinacrine therapy tolerated chloroquine without difficulty. Only one patient in the entire series was unable to continue chloroquine therapy because of repeated nausea and emesis, although the patient's condition was greatly improved by this therapy. Another possible toxic reaction is weight loss. One patient with chronic discoid disseminated lupus erythematosus reported a weight loss of 18 lb. (8.2 kg.) during the 11 week period she received the drug, but she showed great improvement. One patient with subacute disseminated lupus erythematosus had abdominal cramps after each dose, and one with the same form of the disease had diarrhea while taking the drug. Both these patients continued treatment, with improvement in their conditions. Chewing gum has been used to partially relieve the unpleasant aftertaste of which some patients complained. Although three patients in this series had subacute disseminated lupus erythematosus, it is not recommended at present that such patients be included in routine clinical surveys.

Results of Use of Chloroquine Diphosphate in Lupus Erythematosus

Type of Lupus Erythematosus	No. of Patients	Average Duration of Therapy, Wk.	Results: Great Improvement	Results: Improvement	Results: No Change
Chronic discoid localized.....	12	7	7	0	5
Chronic discoid disseminated..	6	11	4	2	0
Subacute disseminated	3	9	3	0	0

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The chloroquine diphosphate used in this study was supplied by Winthrop-Stearns, Inc., New York.

The analyses for chloroquine were done by Dr. Leon H. Schmidt, Director, Institute of Medical Research, Christ Hospital, Cincinnati.

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2. Page, F.: Treatment of Lupus Erythematosus with Mepacrine, Lancet **2**: 755, 1951.

3. (*a*) Wells, G. C.: Treatment of Chronic Discoid Lupus Erythematosus with Atabrine, J. Invest. Dermat. **19**: 405, 1952. (*b*) Sawicky, H. H., and others: Therapeutic Assays of Skin and Cancer Unit of New York University Hospital: Assay 7: Quinacrine Hydrochloride (Atabrine Hydrochloride) for Chronic Discoid Lupus Erythematosus, ibid. **19**: 397, 1952. (*c*) Sulzberger, M. B.: Personal communication to the authors.

4. Schmidt, L.: Personal communication to the authors.

5. (*a*) Berliner, R. W., and others: Studies on the Chemotherapy of the Human Malarias: 6. The Physiological Disposition, Antimalarial Activity, and Toxicity of Several Derivatives of 4-Aminoquinoline, J. Clin. Investigation **27**(pt. 2): 98, 1948. (*b*) Alving, A. S., and others: Studies on the Chronic Toxicity of Chloroquine (SN-7618), ibid. **27** (pt. 2): 60, 1948. (*c*) Chloroquine-Diphosphate—A Newly-Standardized Antimalarial Drug, News and Comment, Bull. U. S. Army M. Dept. **7**: 834, 1947. (*d*) Maier, J.: Field Trial of Chloroquine (SN 7618) as a Suppressive Against Malaria in the Philippines, Am. J. Trop. Med. **28**: 407, 1948.

6. Alving,[5b] Craige, B., Jr., and others: A Lichen-Planus-Like Eruption Occurring During the Course of Chloroquine Administration, J. Clin. Investigation **27** (pt. 2): 56, 1948.

SUMMARY

Preliminary clinical trials have shown chloroquine diphosphate to be of value in the treatment of the chronic discoid phase of lupus erythematosus. This antimalarial agent is less toxic than quinacrine (Atabrine), but, with prolonged administration, the possibility of the occurrence of toxic symptoms must be considered.

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ALLERGIC REACTION TO STREPTOKINASE-STREPTODORNASE SOLUTION GIVEN INTRAPLEURALLY

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and

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The use of streptokinase and streptodornase recently has gained much popularity, especially in the treatment of hemothorax in which clotted blood and fibrinous and purulent accumulations are present. Usually these enzymes are injected intrapleurally in the form of a freshly made sodium chloride solution. They cause a rapid dissolving of the blood clots and fibrinous exudates, thus facilitating removal of the material by aspiration.

Since streptokinase and streptodornase are antigenic, the possibility of the occurrence of dangerous anaphylactoid reactions, especially when the enzymes are injected intrapleurally, should be considered and watched for. Until recently, no severe reactions have been reported, except that in a case in which the outcome was fatal when the drug was injected intrathecally. Literature accompanying the commercial preparations of the product state that allergic reactions have been minimal but nevertheless should be watched for. Carr and Robbins,[1] in a series in which they used combined streptokinase and streptodornase intrapleurally for hemothorax, noted some temperature elevation in all their patients, and 6 of 10 patients complained of pleural pain; all had a feeling of malaise; however, no unusual reactions were noted. In a series of 48 cases, reported elsewhere but summarized by these authors, in which the drug was used similarly, no reactions were noted. Miller and Long [2] did not notice ill effects from the intrapleural administration of the drug in their series of cases. Recently, Baum and Oransky [3] reported an unusual reaction following intrapleural administration of combined streptokinase and streptodornase, which they believed was a pyrogenic and anaphylactoid reaction secondary to the administration of these enzymes. We wish to report a case similar to the one reported by Baum and Oransky, in which the patient's reaction in a subsequent skin test with the solution was strongly positive.

From the Department of Surgery, Columbia Hospital.

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2. Miller, J. M., and Long, P. H.: The Treatment of Hemothorax with Particular Reference to the Use of Streptokinase and Streptodornase, U. S. Armed Forces M. J. **3**: 1061 (July) 1952.

3. Baum, G. L., and Oransky, P.: Unusual Reaction to Intrapleural Administration of Streptokinase and Streptodornase, J. A. M. A. **149**: 1012 (July 12) 1952.

REPORT OF A CASE

A 51-year-old white man entered the hospital Dec. 3, 1952, complaining of pain in the left side of the chest, with shortness of breath, which had begun after an accident in which he had slipped and fallen, injuring his chest wall. A review of the patient's systems and history revealed nothing remarkable. Physical examination on admission revealed a well-developed and well-nourished man in no acute distress. The pulse rate and blood pressure were normal, and there was no external evidence of injury. On examination, the chest showed decreased breath sounds on the left side, with evidence of hemothorax. Initial blood studies showed 3,300,000 red blood cells per cubic millimeter, 10.8 gm. of hemoglobin per 100 cc. (Sheard and Sanford photocolorimeter), and 9,750 white blood cells per cubic millimeter with 64% polymorphonuclears and 36% small lymphocytes.

Results of other laboratory studies were essentially normal. Roentgenograms showed a fracture of the fourth rib on the left in the anterior axillary region and a hydropneumothorax on the left side, with a fluid level at the ninth rib posteriorly. Also, collapse of the left upper lung lobe and partial collapse of the left lower lobe were noted.

Initially, the patient was treated with penicillin intramuscularly and whole blood transfusions. Thoracentesis of the left chest was done about every third day, an average of 300 cc. of dark blood being removed with each aspiration. Since the later aspirations were not satisfactorily removing the blood because of its thickness, it was decided to inject streptokinase-streptodornase solution intrapleurally. On Dec. 15, 1952, after 420 cc. of blood had been aspirated, 100,000 units of streptokinase and 25,000 units of streptodornase in 20 cc. of a sterile isotonic sodium chloride solution was injected through the same needle into the left pleural cavity. A few hours later the patient began to have chills, restlessness, and profuse perspiration. He also had pain in the left side of the chest and complained of shortness of breath. About five hours after the injection, the patient's condition was critical, the blood pressure being 70/40 mm. Hg, the pulse rate 135 beats per minute and weak, the respiratory rate 25, and the temperature 103 F (axillary). No rash was noted. The patient was immediately placed in an oxygen tent. He was given meperidine (Demerol) and 1,500 cc. of plasma, and the dosage of the antibiotic he had been receiving was increased. His condition remained critical, and a few hours later he was given 1,000 cc. of whole blood as well as cardiac stimulants. On the morning of Dec. 16, the patient's condition was still poor; 600 cc. of dark blood was removed easily from the left pleural cavity. Blood studies at this time showed 4,140,000 red blood cells, 12.2 gm. of hemoglobin per 100 cc., and 41,500 white blood cells, with 98% polymorphonuclears and 2% small lymphocytes. A culture of the thoracic fluid at this time was negative for bacteria. That evening, the patient felt a little better; his temperature was 98.2 F (axillary), his pulse rate 112 beats per minute, and his respiratory rate 36. On Dec. 17, an electrocardiogram showed auricular paroxysmal tachycardia, and roentenograms showed a considerable increase in the amount of fluid in the left side of the chest, the upper limit being the fifth interspace posteriorly. The mediastinum and heart were displaced to the right.

After this episode, the patient began to improve. Pleurocenteses were done every two to three days, the fluid aspirated bing less viscous and a little brighter red in color. Much larger quantities were aspirated. The blood cell counts returned to normal. Subsequent roentgenograms showed a decrease in the amount of pleural effusion but also that the left lung had failed to expand fully. The patient was discharged Jan. 3, 1953, in an improved condition.

During examination of the patient about five weeks after the streptokinase-streptodornase injection had been given, a skin test was done. A wheal appeared on the right forearm after injection of the same solution that had been injected intrapleurally. Shortly afterward, severe edema and redness of the entire flexor surface of the forearm, with axillary adenitis, developed. This subsided subsequently with local therapy. The patient will soon undergo a decortication procedure on the left lung.

COMMENT

As stated, the occurrence of reactions after intrapleural use of streptokinase-streptodornase solution has not been common; however, physicians must be on the alert for such a possibility. Since in our patient no skin test was done prior to instillation of the solution, it is not possible to evaluate the significance of the severe reaction to a skin test done five weeks after intrapleural administration of the drug. Despite the increased pleural effusion, as seen in roentgenograms, this case appears to be one of anaphylactoid reaction due to streptokinase and streptodornase rather than one of shock due to hemorrhage and is reported as such.

2244 Milligan Ave. (18) (Dr. Grant).

SEVERE IMMEDIATE CONSTITUTIONAL REACTION TO PENICILLIN

Arthur R. Sohval, M.D., New York

Although unfavorable reactions to penicillin therapy are well known, the occurrence and frequency of serious, life-threatening, immediate constitutional reactions are not generally recognized. The few published reports describe two principal types of prompt systemic reaction. Fatal and near-fatal penicillin anaphylaxis has recently been reviewed by Siegal, Steinhardt, and Gerber.[1] An anaphylactic-like shock state, occasionally fatal, was discussed in a recent issue of THE JOURNAL by Mayer and others,[2] and similar cases have been recorded.[3] An entirely different type of reaction, characterized by sudden weakness and angor animi and with no recognizable evidence of hypersensitivity or circulatory or respiratory disturbance, has been described by Batchelor, Horne, and Rogerson.[4] The fact that Mayer's group observed six cases within a relatively short period of time and Batchelor's group encountered eight cases over an interval of seven months (an incidence of three cases per thousand injections) suggests that severe immediate reactions occur more often than indicated by the relatively few published cases.

This is the report of an alarming reaction that occurred in a patient immediately after intramuscular injection of an aqueous suspension of procaine penicillin. The reaction pattern did not conform to either of the two previously described major types of immediate reaction, although some features of each were manifested.

REPORT OF A CASE

The patient was a 56-year-old physician who had no personal or family history of allergic manifestations. He had received approximately 12 intramuscular injections of procaine penicillin in aqueous suspension for three separate suppurative infections during the previous two years. A questionable skin reaction followed the first injection two years ago. The reaction consisted of a fine desquamation of the palms three to four weeks after the injection. Procaine hydrochloride (Novocaine) has been tolerated without ill effects on numerous occasions. Early in the morning of Feb. 5, 1953, the patient noted malaise and had a slight cough. That afternoon he experienced several shaking chills, and his temperature rapidly rose to 105.8 F. Examination disclosed no etiological findings, and he was given an antipyretic mixture containing acetylsalicylic acid, acetophenetidin, and codeine sulfate. The next morning the patient's temperature was 104 F, and the sputum was blood-tinged. When he was examined at 3 p. m., the temperature was 104.2 F, the pulse 120 per minute, and the respiratory rate 22 per minute. The chest was clear. The leukocyte count was 23,600 per cubic millimeter, of which 39% were nonsegmented, and 53% were segmented polymorphonuclear neutrophils. Because of the sanguinous sputum and the sustained hyperpyrexia, a streptococcic pneumonia was suspected, and antibiotic therapy was instituted. An aqueous suspension of crystalline procaine penicillin G (Crysticillin), containing 600,000 units in 2 ml., was administered intramuscularly in the left buttock with the patient in a prone position. Concurrently, 500 mg. of erythromycin, an antibiotic derived from Streptomyces erythreus, was administered orally, and was to be repeated at six hour intervals. Six hours later the temperature was 103 F, and the pulse and respiratory rates were 118 and 20 per minute respectively. For the first time fine crepitant rales were heard over both lower lung fields posteriorly. Another injection of procaine penicillin G suspension, (Flo-Cillin) 1 million units in 1.7 ml., was given in the right buttock. On the morning of the third day there was marked subjective improvement, and the temperature was 101 F, dropping to 100.2 F in the afternoon. The pulse and respiratory rates were 80 and 20 per minute respectively. Another intramuscular injection of 1 million units of procaine penicillin G suspension in 1.7 ml. was administered in the left buttock. This was given 18 hours after the second injection, and the same technique was used in all three instances, with the usual precaution of withdrawing the syringe plunger prior to injection. There was no reason to suspect penetration of a blood vessel, and the site of injection was not massaged.

Immediately on withdrawal of the needle after the third injection, the patient complained of vertigo, which became more intense as he turned over to the supine position. Simultaneously, he complained of a peculiar metallic taste in his mouth and a sense of nasal obstruction. He also had a feeling of thoracic constriction and warmth as well as severe palpitations. For a few seconds the patient was unable to move his right upper and lower extremities. His speech was slurred, and his tongue felt "thick" for approximately 10 minutes. During this time there was an ashen gray pallor of the face, and the pulse was full and bounding, with a rate of 150 per minute. There was no sweating, faintness, or evidence of bronchial or laryngeal obstruction. The patient displayed intense anxiety and fear of impending death, accompanied by a staring expression and hyperventilation. Overbreathing promptly stopped when it was called to the patient's attention. Since there was no circulatory collapse or respiratory embarrassment, no medication was administered. Recovery from the alarming phase of the reaction (vertigo, hemiparesis, slurred speech, palpitations, thoracic compression, and angor animi) was complete in 15 minutes. The temperature fell to normal levels that evening, and there was rapid clearing of the pulmonary findings under continued administration of erythromycin. A feeling of fatigue persisted for a day. The patient had fully recovered on the eighth day of the illness. Skin sensitivity tests, passive transfer studies, and precipitin reaction tests were not performed.

COMMENT

The reaction pattern in this patient is difficult to classify. It lacked the manifestations of shock, dyspnea, sweating, and disturbances of consciousness that characterize anaphylactic or nitritoid reactions. On the other hand, vertigo, transitory neurological phenomena, an odd taste in the mouth, sense of thoracic compression, and

1. Siegal, S.; Steinhardt, R. W., and Gerber, R.: Fatal and Near-Fatal Penicillin Anaphylaxis: Three New Cases With a Note on Prevention, J. Allergy **24**: 1 (Jan.) 1953.

2. Mayer, P. S., and others: Penicillin Anaphylaxis, J. A. M. A. **151**: 351 (Jan. 31) 1953.

3. Yuval, A.: Reaction to Procaine Penicillin, letter to the editor, Lancet **1**: 163 (Jan. 19) 1952. Smolnikoff, V. P.: Reaction to Procaine Penicillin, letter to the editor, ibid. **1**: 1022 (May 17) 1952.

4. Batchelor, R. C. L.; Horne, G. O., and Rogerson, H. L.: An Unusual Reaction to Procaine Penicillin in Aqueous Suspension, Lancet **2**: 195 (Aug. 4) 1951.

angor animi present in this case have been described in anaphylactic-like reactions to procaine penicillin. Dizziness, weakness, "fluttering in the chest," peculiar taste, and angor animi were also encountered by Batchelor, Horne, and Rogerson [4] in a series of reactions that they believed were entirely nonallergic. So firm was their conviction in this respect that five of their eight patients were subsequently re-treated with the same drug without untoward results.

CONCLUSIONS

In view of the gravity of immediate constitutional reactions to penicillin in its various forms, it is hardly necessary to stress careful selection of patients. Therapeutic indications should be rigid. Screening to eliminate persons with previous histories of untoward penicillin reactions is necessary but is not foolproof. Meticulous attention to injection technique, in order to avoid entry of penicillin into the blood stream, is also essential but does not assure that unrecognized penetration of a vein will not occur. Finally, emergency medication consisting of an injectable vasoconstrictor and an antihistaminic should be immediately available.

It is hoped that more diligent reporting and compilation of casuistic data may lead to an improved understanding of the various pathogenetic mechanisms and to reduction or elimination of serious reactions to penicillin.

ADDENDUM

Since this report was prepared, the problem of immediate anaphylactic reactions to penicillin has received further attention.[5] Severe constitutional reactions were recorded in seven patients with a fatal outcome in five.

1155 Park Ave.

5. Feinberg, S. M.; Feinberg, A. R., and Moran, C. F.: Penicillin Anaphylaxis: Nonfatal and Fatal Reactions, J. A. M. A. **152**: 114 (May 9) 1953.

The Nervous Child.—The discussion deals with an amorphous group whose symptoms are not definite enough to be dignified with such titles as anxiety neurosis et cetera. The mother will say that he is very highly strung or that his nerves are bad; that he is too sensitive; that he is prone to tears. . . . The teacher may complain that the child is restless, cannot concentrate or fix his attention. Various behaviour disorders may be added to the picture; habit disorders such as stammering, bed-wetting, nail-biting, skin-picking and masturbation appear from time to time. . . . These children are just too soft and give excessive emotional response to ordinary stimuli. They need to be toughened and to be assisted to acquire reasonable emotional control. The phrase used as the title, "The Nervous Child" has a bad influence. When a parent is told that his child has bad nerves, it conveys to him that there is a disease process in very vital tissues. And disease calls for protection. With the added protection the subject becomes still more sensitive. Thus a vicious circle is established. . . . Yet, if one can convey to the parent that his child is emotionally ill while the nervous system is organically quite sound, it produces an entirely different orientation. Instead of looking for direct intervention by the doctor, he will begin to seek for factors in the environment. . . . One must especially guard against a sudden change from coddling to a Spartan regime. One may point out that a limb which has been protected by a splint for any length of time will be very soft and sensitive at first. It will need carefully graded exercises until it gradually regains its strength and is able to function like the normal one. A hothouse plant, if suddenly exposed to the elements, will succumb; but if protection is withdrawn little by little the adaptation process will go on until the hothouse plant becomes as tough as the plant that grew outside from the beginning.—H. M. North, M.D., The Nervous Child, *Medical Journal of Australia*, May 2, 1953.

A SYRINGE SHIELD USED IN INJECTING RADIOACTIVE GOLD

Paul Getzoff, M.D.
John Hidalgo, M.S.
and
Joe Meyer, Ph.D., New Orleans

Since the introduction by Flocks and others [1] of the concept and technique of employing radioactive gold (AU^{198}) in the treatment of prostatic carcinoma, we have been interested in this fresh approach and the promising results obtained. We have found Flocks' operative method completely satisfactory. The technique for concentrating a solution of radioactive gold in the prostate gland consists of the direct injection of the material into the organ suprapubically, retropubically, and through a spinal needle inserted perineally. Obviously, certain problems are involved with any method that includes use of radioactive isotopes.

The broad principles involved in this operation may be briefly summarized as follows: 1. The radioactive gold must be injected in such a manner as to assure maximum diffusion of the solution throughout the prostate gland. 2. Retrograde leakage through the tract produced by the needle should be minimal. 3. Depth of the injection must be completely controlled so that the rectal wall is not penetrated. 4. The surgeon, his assistants, and other operating room personnel who handle the "hot" syringe must be guaranteed reasonable safety.

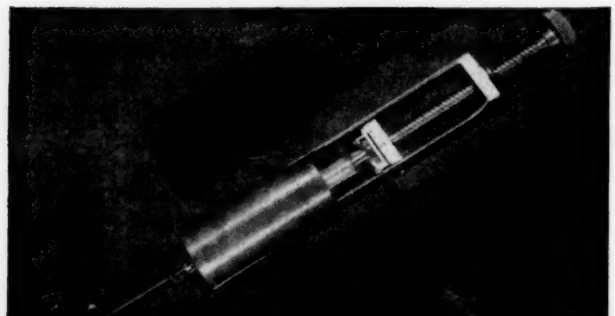
We have designed and used successfully a simple syringe shield constructed to fulfill the requirements described. When the radioactive gold solution is injected with various syringes, the stony indurated character of the malignant prostatic tissue is manifested by the difficulty encountered in forcing the solution into the glandular substance. Our apparatus has considerable mechanical advantage. The surgeon is able to inject the solution with almost "finger tip" ease and with both mechanical preciseness and a minimal loss of the solution by leakage back into the bladder through the sites of injection. The screwing motion of injection obviates the possibility of "binding" between the plunger and barrel of the syringe and minimizes the danger of the syringe breaking during the injection. The latter has been a frequent occurrence with ordinary syringes. Safety factors, which are of inestimable importance in the handling of radioactive material, are preserved. The syringe is handled with complete ease by the physicist and operating personnel. This instrument is easily made by a skilled machinist. It is economical, sturdy, easy to clean, and can be conveniently assembled and disassembled in a few seconds.

An additional feature is the guard placed on the needle. Spinal needles (19 gage) are fitted with easily adjustable guards that resemble the type used on ornamental tie pins. The desired depth of injection is estimated, and the guard is adjusted accordingly by the

From the departments of urology and biophysics, Touro Infirmary, the Department of Physics, Tulane University, and the Radioisotope Unit, Veterans Administration Hospital, New Orleans.

1. Flocks, R. H.; Kerr, H. D.; Elkins, H. B., and Culp, D.: Treatment of Carcinoma of the Prostate by Interstitial Radiation with Radio-Active Gold (Au198): Preliminary Report, J. Urol. **68**: 510-522, 1952.

physicist in charge of filling the syringes. Several needles are kept available with the guards adjusted to suit variable conditions in the same patient. The use of these needle guards has made possible greater accuracy and safety in injections into nodular glands where the penetration distance differs at various sites.



A, shield enclosing syringe for injection of radioactive gold solution; *B*, shield, syringe, and needle with adjustable guard.

The outside diameter of the shield is 1⅞ in. A 10 cc. Luer-Lok syringe is surrounded by a shield of lead 7/16 in. thick and encased in a brass tube ⅛ in thick. The drive screw is double threaded, with a ¼ in. pitch providing a mechanical advantage of 5.5×. The syringe plunger is 0.25 square in. in cross section. This adds a factor of 4× for pressure units. Thus, a force of 1 lb. exerted on the perimeter of the screw will yield 5.5 (mechanical advantage of drive screw) × 4 (pressure units factor) × 1 (lb. of exerted pressure) = 220 lb. per square inch. The knob also adds some mechanical advantage. It has a diameter of 1½ in. and a radius of 7/32 (0.218) in. A ratio of the imparted force (F) to the resultant force (R) is a measure of the effective radii.

$$\frac{F}{0.625} = \frac{R}{0.218}$$

$$\frac{F}{R} = \frac{0.625}{0.218} = 2.87$$

Mechanical advantage obtained with 1 lb. of pressure applied to the perimeter of the screw is as follows:

Mechanical advantage $22.0 \times 2.87 = 63.1 \times$

The markings on the guide bar are calibrated into 10 divisions indicating 1 cc. each. This enables the physician to measure with reasonable accuracy (i. e., by observing the pointer) the millicuries in the solution being injected.

SUMMARY

A new and simple type of syringe shield is described for use in the injection of radioactive gold (Au^{198}) in carcinoma of the prostate gland as described by Flocks and others.[1] The device is economical and is devoid of complicated delicate adjustments.

This apparatus makes possible effective, safe, accurate, and relatively easy injection by virtue of its high mechanical advantage (63.1 ×). Its value is further enhanced by an adjustable guard placed on the needle, which prevents the insertion of the needle beyond a predetermined point.

3439 Prytania St. (Dr. Getzoff).

SALMONELLA MONTEVIDEO INFECTION FOLLOWING USE OF POWDERED EGG YOLK

Capt. Samuel C. Southard (MC), Army of U. S.
Major Walter B. Watson
and
Capt. Arnold J. Capute, (MC), U. S. Army

The following case of Salmonella montevideo infection is reported because of the unusual probable source of infection, dry powdered egg yolk. In giving treatment for or attempting to prevent recurrences of such infections, physicians should consider this possible source. A letter was sent to the packing company to determine whether this strain of S. montevideo had been isolated from their product, dry powdered egg yolk. They replied immediately that they had been informed by the Federal Food and Drug Administration that S. montevideo had been recovered from the dry egg yolk tested in the Food and Drug Administration laboratories but that this finding had not yet been confirmed by their own laboratories.

REPORT OF A CASE

A 3-year-old white girl was admitted Nov. 13, 1952, to the pediatric service of the U. S. Army Hospital, Fort Hamilton, Brooklyn, N. Y., with the chief complaint of diarrhea. The patient had been under the care of this hospital's pediatric service for the previous year and had been known to have incomplete cystic fibrosis of the pancreas. She had been doing well and had been gaining weight by following a celiac type of diet, until four days prior to admission, when she vomited once. She had no other symptoms until diarrhea began two days prior to admission. This consisted of loose, dark brown to black, watery stools, with a small amount of thick mucus. At this point, the patient was seen by another physician, who prescribed dietary restrictions and administration of a kaolin mixture and 300,000 units of procaine penicillin intramuscularly. The white blood cell count at that time was 10,200 per cubic millimeter, with 84% neutrophils and 16% lymphocytes. The following day, diarrhea became more profuse, and the father, a physician, noted what appeared to be streaks of bright red blood. Because of the patient's history of cystic fibrosis, she was admitted to the hospital.

Physical examination on admission revealed a thin, poorly nourished child weighing 25 lb. (11.3 kg.). The throat, fauces, and tonsils were injected. The temperature was 101.4 F. The child was put to bed, was placed on an appropriate constipating diet, and was given procaine penicillin, 300,000 units intramuscularly every 12 hours. The diarrhea subsided in 24 hours. The temperature returned to normal in 48 hours, remained normal for 48 hours, and then returned to 101 F, with recurrence of the pharyngitis. This responded without difficulty to administration of additional penicillin and the usual symptomatic treatment. Results of urinalysis were normal. The white blood cell count showed a slight increase of the neutrophils but was otherwise within normal limits. A throat culture showed a hemolytic strain of type A beta hemolytic Streptococcus and a hemolytic strain of Staphylococcus aureus. Stool examination showed the presence of gross blood, and culture showed the presence of a strain of Salmonella organisms. This culture was sent to the First Army

From the Pediatric Service, U. S. Army Hospital, Fort Hamilton, Brooklyn, N. Y.

Dr. Southard has been released from the Army and is now practicing in Ventnor City, N. J.

Medical Laboratory, where the strain was identified as S. montevideo. The child was then given a mixture of sulfadiazine and sulfamerazine while awaiting the results of sensitivity tests of the S. montevideo isolated.

Family history revealed that on Nov. 6, 1952, the girl's younger brother, aged 11 months, had had a short episode of mild diarrhea, which was treated successfully with dietary restriction and use of a kaolin mixture. On Nov. 9, the patient's mother also had a short episode of mild diarrhea, which subsided after two days without therapy. Concomitantly with the hospitalization of the 3-year-old girl, a survey of the family revealed that the patient's 11-month-old brother and her father also harbored the same strain of bacteria. The infant was admitted to the hospital to receive therapy in an attempt to abolish the carrier state. It is interesting to note that this family first used powdered dried egg yolk for the infant on about Nov. 1, 1952, and six days later diarrhea developed in him.

Sensitivity tests (broth dilution method) showed that this strain of S. montevideo was not inhibited by bacitracin, penicillin, or the sulfonamide mixture. Slight inhibitions were produced by concentrations of 10 μg per cubic centimeter of aureomycin, 30 μg per cubic centimeter of oxytetracycline (Terramycin), and 10 μg per cubic centimeter of chloramphenicol. Inhibition was produced by a concentration of 10 μg per cubic centimeter of dihydrostreptomycin. Cultures were again made, and the organisms were found to persist despite sulfonamide therapy, as was expected from the sensitivity tests.

Both children were then given 1 gm. of streptomycin orally per day in two equal doses every 12 hours. This was continued arbitrarily for five days. After a waiting period of three days, cultures were again made. Three daily cultures were negative for Salmonella. The father also took streptomycin orally under the direction of his physician. This family will be followed for six months to make certain that the carrier state has been abolished.

SUMMARY

A case of Salmonella montevideo infection in a 3-year-old girl following use of powdered egg yolk is reported. The child's father and infant brother were also found to be harboring the organism, which was shown to be sensitive to streptomycin. All three were treated and will be followed until the carrier state has been eliminated.

7217 Atlantic Ave., Ventnor City, N. J. (Dr. Southard).

Today's Family Doctor.—Pendulums inevitably swing too far and then come back. Today the swing is back to a proper regard for the family physician. We might say a proper regard for the new family physician. Who is this new family physician? He is a man or woman who has completed six years in university study and has spent an average of two years in hospital training, following graduation. He is well versed in modern methods of diagnosis and treatment. He knows his limitations in treating cases which may require specialist care. He takes time off each week for study in his neighborhood hospital and each year takes a refresher course in some aspect of his work. He is fully trained in the aspect of medicine which reveals nearly every disease—the ability to evaluate the patient's story about his illness, and the ability to do a thorough physical examination. Relatively few cases require diagnostic aids other than those in daily use in the family doctor's office; and relatively few cases require treatment other than that which the family doctor is able to give.—G. I. Sawyer, M.D., Every Family Needs a Doctor, *Health*, May-June, 1953.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

APPARATUS ACCEPTED

The following additional products have been accepted as conforming to the rules of the Council on Physical Medicine and Rehabilitation of the American Medical Association for inclusion in Apparatus Accepted. A copy of the rules on which the Council bases its action will be sent on application.

RALPH E. DE FOREST, M.D., *Secretary.*

Multitone Muscle Stimulator, Model 3

Bilton Laboratories, Inc., 100 S. Broad St., Philadelphia 10.

The Multitone Muscle Stimulator, Model 3, is an apparatus for generating electric currents to stimulate innervated voluntary muscles as an aid in rehabilitation, to retard muscle atrophy, and to prevent adhesions and joint atrophy in patients who cannot exercise voluntarily. The apparatus weighs 11.3 kg. (25 lb.) and is portable. It requires a source of 60-cycle alternating current at 110 volts and draws 22 watts.

Multitone Muscle Stimulator, Model 3

It is equipped with eight circular electrodes so that more than one muscle can be exercised at a time. A selector switch set at "Push-Pull" energizes the right and left circuits alternately and thus makes it possible to elicit reciprocating contractions of antagonistic muscle pairs. Other controls permit adjustment of intensities and frequencies. The apparatus is accepted for use under medical supervision in stimulating normally innervated muscles.

Ille Mobile Sitz Bath, Model SB 100

Ille Electric Corporation, 50 Mill Road, Freeport, Long Island, N. Y.

The Ille Mobile Sitz Bath is a metal chair with the seat modified for application of heated water to the perineal region. It is intended for use in treatment or postoperative care in gynecologic, obstetric, and rectal cases. A heater maintains the temperature of the water during the interval between filling of the bath and immersion of the part to be treated. The heating unit operates on either direct or alternating current at 115 volts and draws 325 watts.

Ille Mobile Sitz Bath, Model SB 100

The chair frame is made of aluminum tubing; the water pan is of stainless steel. The unpacked article weighs 13.6 kg. (30 lb.) and measures 89 by 74 by 61 cm. (35 by 29 by 24 in.). Packed for shipment it measures 102 by 76 by 76 cm. (40 by 30 by 30 in.) and weighs 38.6 kg. (85 lb.). The apparatus has the approval of Underwriters' Laboratories, Inc.

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TRANSFUSION OF PLATELETS

Uncontrolled hemorrhage due to thrombocytopenia may occur not only in essential thrombocytopenia but also in secondary thrombocytopenia such as may follow treatment of leukemia with myelotoxic agents or exposure to ionizing radiation. Such a hemorrhage responds poorly to transfusion of blood obtained from blood banks, presumably because the platelets are quite unstable under the conditions of collection and storage. Consequently, in recent years attention has been directed toward development of improved methods for the collection, storage, and administration of platelets. The current status of this work has been reviewed by Stefanini and Dameshek [1] together with a summary of their clinical experiences over a three year period.

Stefanini and Dameshek point out that in ordinary blood bank procedures agglutination and destruction of platelets is favored by their contact with such foreign surfaces as glass and metal and by the foaming that may result from the use of a vacuum. Indeed, it has been found that transfusions of blood obtained from blood banks do not elevate the platelet counts of thrombocytopenic recipients appreciably.

Several technical procedures are now available, however, that permit increased survival of platelets in vitro and in vivo. Thus a number of materials are available for coating metal surfaces or glassware with nonwettable endothelial-like surfaces [2] such as Arquad 2-C (dicocodimethyl-ammonium chloride) for coating needles, silicone lacquer, and Teflon fluid (a tetrafluoroethylene resin preparation) for coating metal surfaces, and silicone (methyl-chloro-silane) for coating glassware. Collection of blood without great loss of platelets is possible if such coated metal and glassware are used as well as tubes of nonwettable plastic or equipment made entirely of plastic. A new anticoagulant, Sequesterene disodium (disodium ethylenediamine tetra-acetate), minimizes the tendency of platelets to become sticky, to agglutinate rapidly, and to undergo morphological alterations in shed blood.[3] Other measures for more efficient separation and concentration of platelets include the use of surface acting agents such as polysorbate 80 (Tween-80) and Triton WR-1339 (an alkylaryl polyether alcohol) to reduce irreversible agglutination of platelets [4] and of ion-exchange resins such as Dowex-50 for the removal of platelets from blood. The resins trap the platelets as the blood that flows through is decalcified and made incoagulable. Platelets can then be recovered by elution.[5]

The clinical work described by Stefanini and Dameshek is based on a total of 216 platelet transfusions in 83 patients. Of these patients, 45 had idiopathic thrombocytopenia purpura, 33 had "amegakaryocytic" secondary thrombocytopenic purpura, and 5 had "hypersplenic" thrombocytopenic purpura. Platelet transfusions were given by various methods, including the transfusion of polycythemic blood or plasma directly with the use of multiple silicone-coated syringes, the transfusion of blood or plasma from polycythemic donors collected in and administered by plastic sets or silicone-coated glass bottles and plastic tubing, and the administration of concentrates of platelets isolated by multiple low speed centrifugation of whole blood collected by gravity in silicone-coated glassware with Sequestrene disodium used as the anticoagulant.

In comparing these methods it was found that when comparable numbers of platelets were transfused into patients with secondary thrombocytopenia, the platelets survived longest (four to five days) when platelet-rich polycythemic blood was transfused directly. The second longest survival period was with polycythemic blood collected in silicone-coated bottles or plastic bags. Platelets survived for much shorter times when they were separated and resuspended in their own plasma, while almost no platelets survived when they were resuspended in saline solution before being administered. These results agree well with results of in vitro studies, which demonstrated, among other things, that platelets that were resuspended in plasma still had the ability to normalize the clot retraction of platelet-poor plasma after they had been stored for 10 days at 51 C, while platelets that were resuspended in saline solution lost this ability after 10 to 24 hours.

Stefanini and his co-workers have found that administration of platelets to patients with either a quantitative or a qualitative platelet deficiency results in more complete retraction of the clot, reduction of the bleeding time, more complete utilization of prothombin during clotting, and improvement of the capillary fragility and of the bleeding manifestations. While better results were obtained with platelet-rich blood or plasma than with isolated platelets, in all cases the effects were manifested for some time after the injected platelets had disappeared from the circulation. This finding suggests that the hemostatic effect of platelets is due, in part at least, to relatively stable constituents of platelets liberated when these bodies integrate.

1. Stefanini, M., and Dameshek, W.: Collection, Preservation and Transfusion of Platelets with Special Reference to Factors Affecting "Survival Rate" and Clinical Effectiveness of Transfused Platelets, New England J. Med. **248**: 797-802, 1953.

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The value of platelet transfusions is limited by the fact that the survival of platelets in vivo is considerably reduced by the pathological state of the recipient. Stefanini and his associates feel that this response is in some cases nonspecific, but in others a platelet-destructive mechanism appears to be the important factor. Survival of transfused platelets is greatly reduced in severe transfusion reactions and in severe, uncontrolled hemorrhage. Splenomegaly, irrespective of its etiology, may cause fast disappearance of platelets. Platelet-destructive mechanisms are present in idiopathic thrombocytopenic purpura and in thrombocytopenia due to drug sensitivity when the causative drug is still in the circulation. Furthermore, repeated transfusions of platelets or platelet products may give rise to decreased platelet survival owing to the appearance of platelet agglutinins. It is possible that this is due to the administration of mismatched thrombocytes, since preliminary evidence suggests there may be platelet groups in human beings.

The results thus far obtained with the use of platelet transfusions would seem to justify a continued search for better methods of platelet isolation and for the identification of the factor or factors in platelets responsible for their hemostatic effects. Such studies not only offer a promising therapeutic approach but may well throw further light on the pathogenetic mechanisms in certain thrombocytopenic states.

THE BIOSYNTHESIS OF CHOLESTEROL

The availability of isotopes for "labeling" suspected precursors of biologically important substances made possible the fundamental discovery that the simple, abundant 2-carbon compound, acetate, is used in the biosynthesis of cholesterol.[1] Atoms of radioactive carbon (C^{14}) derived from acetate administered to experimental animals were found to appear in the cholesterol subsequently isolated from the tissues. Recent work has further demonstrated that the synthesis of cholesterol from acetate proceeds by way of the cyclization of the hydrocarbon squalene.[2] The site and the regulation of the biosynthesis of cholesterol are also problems of great medical interest and fundamental importance. The liver appears to be the primary locus of cholesterol synthesis in the adult,[3] whereas other tissues, including the kidney, testes, adrenal cortex, ovaries, and small intestine, are active in the fetus.[4] The skin also contributes somewhat to cholesterol synthesis in the adult.

A number of factors have been shown to affect the rate of synthesis of cholesterol, particularly in the liver. One of the most interesting of these is cholesterol itself.[5] With liver slices to which C^{14}-acetate was added, the rate of hepatic synthesis of cholesterol was carefully followed in control, untreated dogs and in dogs previously fed relatively large amounts of cholesterol. A very low rate of synthesis was found in the cholesterol-fed group. This observation is perhaps not an unexpected one. The presence or accumulation of the end-product of most reactions, particularly enzymatic, inhibits any further reaction. As another example, the continued administration of a hormone is typically attended by a decreased production of the same hormone by the endocrine gland involved, even to the point of atrophy of the secretory tissue. In the case of cholesterol, this is perhaps a fortunate coincidence in the protection of the organism against an oversupply of cholesterol and in maintaining homeostasis with respect to this sterol. Furthermore, these observations may add to the now considerable amount of evidence indicating that an increased cholesterol intake is not an etiological factor in supposed aberrations of cholesterol metabolism, such as atherosclerosis.

Two other important factors affecting the biosynthesis of cholesterol are being studied currently. One of these is pantothenic acid.[6] In studies on rats, a group of California investigators observed that there is a decreased synthesis of cholesterol by the liver in pantothenic acid deficiency. This is a rather reasonable finding, since pantothenic acid is a constituent of coenzyme A, which is required for the metabolism of acetate, which, in turn, serves as a precursor of cholesterol as mentioned above.

A second vitamin currently indicated to be involved in the regulation of cholesterol formation, at least in the adrenal, is ascorbic acid.[7] The preliminary results show that the adrenal glands of the severely scorbutic guinea pig incorporate six times as much C^{14}-labeled acetate into cholesterol as do those of normal control animals under otherwise identical conditions.

The recent studies described above indicate that the biosynthesis of cholesterol is a delicately controlled mechanism that is not only adapted, on the one hand, to insure an adequate supply of this extremely important essential metabolite in the body but also regulated, on the other hand, to prevent an oversynthesis in potentially dangerous amounts.

PATHOGENESIS OF ESSENTIAL HYPERTENSION

The pathogenesis of essential hypertension, which accounts for 95% of the cases of hypertension seen clinically, is still unknown in spite of extensive clinical and laboratory studies during the past 20 years. However, these studies have indicated neurogenic, endocrine (anterior pituitary–adrenal cortex), and renal changes in pathophysiology that may have pathogenetic significance. Thus some patients with essential hypertension show evidence of increased vasomotor tone, others show mild disturbances in water and sodium chloride metabolisms, and some show increased plasma concentrations

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of vasoexcitatory material (VEM) and vasodepressor material (VDM), produced by the kidney and liver, respectively. Whether these changes connote several pathogenetically distinct types of hypertension or whether essential hypertension is a single clinical entity with varying degrees of alteration in different body functions remains to be determined.

Since the pathogenesis of essential hypertension is unknown, treatment is based on pathophysiology and empiricism. Moreover, information about the long-term effects of presently recognized methods of treatment (psychotherapy, sedatives, low salt diet, autonomic drugs, and sympathectomy) on the basic hypertensive vascular disease process is incomplete and largely limited to sympathectomy. That these types of therapy afford symptomatic relief in some patients has been amply demonstrated; that they prolong life in some is probable; but that they are capable of delaying the progress of the basic cardiovascular disease in most patients can only be conjectured at present. Since all these methods of treatment have an antihypertensive effect in certain patients and hypertension is known to accelerate the onset and accentuate the progress of atherosclerosis and arteriolosclerosis, long-term antihypertensive therapy should at least decrease the incidence and severity of arteriosclerosis in essential hypertension.

The reproduction of a disease in experimental animals has almost invariably led to better understanding of the disease and hence to better therapy. Accordingly, many attempts have been made to reproduce essential hypertension experimentally. Thus far, these efforts have resulted in important progress rather than complete success. Section of the carotid sinus and aortic depressor nerves is very efficient in producing hypertension due to increased vasomotor tone; however, this hypertension is characterized by tachycardia and absent buffer nerve function and, therefore, differs importantly from essential hypertension. Large doses of crude anterior pituitary extract or of its somatotropic hormone and large amounts of desoxycorticosterone acetate and sodium chloride produce hypertension in rats but not in dogs. This hypertension, however, resembles that of pituitary basophilism and adrenal cortical tumors, rather than essential hypertension. Partial constriction of the renal arteries in all species of animals studied produces hypertension [1] that in all important respects thus far studied resembles essential hypertension. Obviously it cannot be concluded that these similarities indicate even a partial common pathogenesis for the two conditions, but the similarities encourage study of the pathogenesis and treatment of experimental renal hypertension in the hope that the enigma of essential hypertension will be brought nearer to solution.

Although 20 years have passed since Goldblatt first produced experimental renal hypertension, its pathogenesis is still unsettled. The three principal hypotheses are alteration in the renin-angiotonin (hypertensin) mechanism, decreased secretion of a renal blood pressure regulating hormone, and increased formation of pressor amines by the kidney. Recently a research group at the University of Illinois College of Medicine offered good evidence that renin or a closely related renal protein is pathogenetic in experimental renal hypertension in dogs.[2] Experiments extending over more than a decade demonstrated that repeated injections of hog renin into dogs produced an antibody (antirenin) that neutralized the pressor effect of hog renin and also dog renin. Experimentally induced renal hypertension in dogs was successfully treated with hog renin and also prevented by prophylaxis with hog renin. The therapeutic and prophylactic effects were well correlated with the antirenin titer. Control tissue extracts were without antihypertensive effect. The same research group subsequently found that the passive transfer of high titer antiserum to dogs with chronic renal hypertension produced a significant antihypertensive effect that was also well correlated with the antirenin titer.[3] Even more important, perhaps, is the finding that similar renin-antirenin treatment of spontaneous hypertension in the dog (which may be the counterpart of essential hypertension in man) produced excellent antihypertensive effects.[4]

Unfortunately, antirenin to hog renin does not neutralize monkey or human renins; hence, semipurified hog renin was without antihypertensive effect in experimental renal hypertension in the monkey, even in the presence of good antirenin titers.[5] Negative results were also obtained with hog renin in essential hypertension, as was to be expected even if the pathogenesis of essential hypertension should ultimately prove to be primarily on a renal renin basis.[6] However, the finding that a passively produced antirenin titer is similarly effective in its antihypertensive action to a titer actively produced in chronic renal hypertensive dogs suggests a heretofore unavailable method for determining what proportion, if any, of patients with essential hypertension have hypertension on a renal renin basis. The University of Illinois group has shown that antirenin to human renin produced in the rabbit, dog, and goat neutralizes human renin. After preliminary studies in the monkey, they propose to study the effect of the passive transfer of purified antirenin to human renin in essential hypertension. Significant antihypertensive effects would suggest a pathogenetic role for the kidney and the renin mechanism. Should essential hypertension in an appreciable percentage of patients prove to be primarily on a renal renin basis, research groups that are not now interested in the problem might well be stimulated to alter the antigenicity of hog renin or other animal renins to overcome the species difference that presently precludes the possible successful use of these renins in the treatment of hypertension in human patients.

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MEDICAL NEWS

CALIFORNIA

Dr. Guedel Honored.—At the Third Biennial Western Conference of Anesthesiologists, Dr. Ralph T. Knight, Minneapolis, president, American Society of Anesthesiologists, acting on behalf of the Cuban Society of Anesthesiology, presented to Dr. Arthur E. Guedel, emeritus associate clinical professor of surgery (anesthesiology) at the University of Southern California School of Medicine, Los Angeles, a scroll testifying his election to honorary membership in the Cuban society. Dr. Georgina A. Funtanellas, graduate of the University of Havana Faculty of Medicine and Pharmacy, and now head of the department of anesthesiology at the San Francisco Hospital, represented the Cuban society.

Course on Radioisotopes.—The University of California Extension offers a course in "Fundamental Principles of Radioactivity Including Clinical Use of Radioisotopes," directed particularly toward the clinical and experimental use of radioisotopes and designed to meet the requirements of the Atomic Energy Commission in respect to distribution of radioisotopes. On satisfactory completion of the course, students will be able to obtain radioisotopes directly from the Atomic Energy Commission. The 40 week course involves laboratory and lecture sessions on Wednesdays from 7 to 10 p. m., beginning Sept. 16, and clinical sessions on Wednesdays from 9 to 12 a. m. and 2 to 5 p. m., May 12 to June 30, 1954 (10 all-day sessions). Primary emphasis will be placed on laboratory work including experiments with radioisotopes as well as radioactivity detecting and counting techniques. Fee for the course is $700. The course is limited to 12 registrants, who must be graduates of approved medical schools. Application or requests for information should be made to Dr. Thomas H. Sternberg, Head of Postgraduate Instruction, Medical Extension, University of California, Los Angeles 24. Study sessions will be held at the university's School of Medicine, 10975 Wilshire Blvd., Los Angeles 24, with clinical sessions at Wadsworth General Hospital, Veterans Administration Center, Los Angeles, and Harbor General Hospital in Torrance.

GEORGIA

Narcotic Violation.—Dr. Marvin A. Acree, Calhoun, pleaded guilty in the U. S. District Court at Rome, June 3, to a violation of the federal narcotic law and on the same date was sentenced to three years' probation and was fined $500.

Society News.—The Georgia Urological Society has elected the following officers: Dr. James L. Pittman, Atlanta, president; Dr. J. Robert Rinker, Augusta, president-elect; and Dr. J. Zeb McDaniel, Albany, secretary-treasurer.——The Georgia Society of Ophthalmology and Otolaryngology has elected Dr. W. Eugene Matthews, Augusta, president; Dr. J. Kirk Train, Savannah, vice-president; and Dr. Alton V. Hallum, Atlanta, secretary-treasurer. The society's spring meeting in 1954 will be held March 5-6 at the General Oglethorpe Hotel, Savannah.

ILLINOIS

School for the Blind Teaches by Mail.—The Hadley Correspondence School for the Blind, Winnetka, will attempt to raise $115,000 in 1953 in order to erect a building to house its institution, which has grown from one pupil in 1921 to its present 1,100 in 48 states and 27 foreign countries. The school, founded by a blind Chicago high school teacher, Mr. William A. Hadley, offers some 70 courses, in addition to the fundamental lessons of Braille. No tuition is charged, the school being maintained solely through the support of interested persons.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

Hospital News.—According to a recent report from the Bureau of Hospitals, State Department of Public Health, during the past decade the birth rate in Illinois hospitals has increased markedly, 197,750 babies having been born last year in Illinois hospitals licensed for maternity service, compared with 136,648 in 1943. About 98 of every 100 births in Illinois last year occurred in hospitals. As for the reduction in maternal mortality in hospitals, 77 mothers died last year from complications associated with childbirth, compared with 286 such deaths in 1943. The maternal mortality rate in hospitals declined from 21.4 deaths per 10,000 live births in 1943 to 4 in 1952. Infant mortality under one month of age fell from about 22 per 1,000 live births in 1943 to 17.7 last year.

Chicago

Cancer Gift.—A check for $1,000 recently presented to Dr. John A. Rogers, executive director of the Illinois Division, American Cancer Society, represented funds raised by the Philip Solomon Memorial Club.

Society News.—At the annual meeting the Chicago Gynecological Society elected the following officers: president, Dr. Henry Buxbaum; president-elect, Dr. Jacob P. Greenhill; vice-president, Dr. John R. Wolff; treasurer, Dr. Harry Boysen; secretary, Dr. Edwin J. DeCosta; pathologist, Dr. Arthur H. Klawans; and editor, Dr. Magnus P. Urnes.——The Chicago Society of Allergy has elected Dr. Abraham L. Aaronson, Chicago, president, Dr. Max Samter, Oak Park, Ill., president-elect, and Dr. Simon S. Rubin, Gary, Ind., secretary-treasurer.

Personal.—At a ceremony in the nurses' residence of Michael Reese Hospital, a plaque was awarded to Dr. Isaac A. Abt "in honor of his outstanding contributions to the science of healing sick children." Dr. Abt is one of the founders of the Sarah Morris Hospital for Children at Michael Reese.——Friends and fellow members of the Rush Medical alumni of the University of Chicago recently honored Dr. Ottilie Zelezny Baumrucker of the Women's and Children's Hospital for her 50 years in the practice of medicine. She was feted at a dinner in the Shoreland Hotel.——Dr. Meyer R. Lichtenstein has been named medical director of the City of Chicago Municipal Tuberculosis Sanitarium succeeding Dr. Otto L. Bettag, who resigned in January to become director of the Illinois Department of Public Welfare. Dr. Lichtenstein has been serving as acting medical director in addition to his regular duties as chief of the medical department.——Dr. Abraham Levinson, professor of pediatrics, Northwestern University Medical School, recently delivered the first annual Dr. B. Bernard Weinstein History of Medicine Lecture in New Orleans. The lecture was sponsored by the Tulane History of Medicine Society in honor of Dr. Weinstein, who is associate professor of clinical gynecology at Tulane University of Louisiana School of Medicine and faculty adviser to the society.——Dr. Earl H. Blair, deputy director for health services of the Chicago Civil Defense Corps, has been named as one of 65 volunteer civil defense workers in 34 states to receive the 1953 Freedoms Foundation civil defense awards for "rendering paramount service toward maintaining the American way of life."

KANSAS

Arkansas City Fluoridates Water Supply.—On June 11, Arkansas City became the 15th Kansas city now fluoridating public water supplies. Fluoridation of the municipal water supply in Arkansas City was endorsed by the Arkansas City and Cowley County dental societies. Other towns in Kansas now fluoridating the public water supply are Ottawa, Horton, Junction City, Garnett, Seneca, Fort Scott, Minneapolis, Hays, El Dorado, Coffeyville, Iola, Colony, Lawrence, and Paola.

University News.—Dr. Vernon E. Wilson, who recently completed his internship in the University of Illinois Research and Educational Hospitals, Chicago, has been appointed assistant dean in charge of student affairs at Kansas University Medical Center, Kansas City. Dr. Wilson, who will also be assistant professor of pharmacology, will assume his new duties Sept. 1.

Personal.—Dr. Lester A. Latimer, who has practiced medicine in Alexander for 43 years, was recently honored by his community at a farewell program in the high school auditorium. The plaque presented to Dr. Latimer in appreciation of his service contains an engraved bronze inscription to Dr. and Mrs. Latimer and a picture of the home that they occupied in Alexander for 25 years and which they are leaving for a new home in Kansas City, where Dr. Latimer will spend his retirement.——Dr. Mowry S. Thatcher of Turon was recently honored with a dinner and program at the Turon High School, given by the community that he has served for over 50 years.——Dr. Samuel T. Coughlin has been elected president of the medical staff of St. Joseph Memorial Hospital, Larned.——Dr. John M. Anderson, superintendent of the Topeka State Hospital, has resigned and will enter private practice in Atlanta.——Dr. Philip A. Bearg has been appointed pediatrician on the staff of the division of maternal and child health, Kansas State Board of Health, Topeka. He previously served as an epidemiologist in the New Haven (Conn.) City Health Department, then was commissioned as passed assistant surgeon in the Public Health Service Reserve Corps, and assigned to the California State Department of Health from 1943 to 1945, when he became health officer of San Luis Obispo, Calif.——Dr. Karl A. Menninger, Topeka, director of education for the Menninger Foundation, was recently honored by the Topeka Chapter of the National Conference of Christians and Jews as the Topekan who had contributed notably to the cause of world brotherhood. The annual citation was presented at the Brotherhood Banquet.

MARYLAND

Dr. Reed Named Hopkins President.—Lowell J. Reed, Ph.D., whose retirement as vice-president of the Johns Hopkins University and Hospital was recently announced (*J. A. M. A.* **152:**1347 [Aug. 1] 1953), has reconsidered his decision to retire and has accepted appointment as president of the university to succeed Detlev W. Bronk, Ph.D., who has been appointed president and chief executive officer of the Rockefeller Institute for Medical Research in New York. In announcing Dr. Reed's appointment, Mr. Carlyle Barton, president of the board of trustees, said: "Dr. Reed's part in developing the present programs of the university, his long association with the faculties and his achievements as a teacher, scientist, and administrator assure us that during his incumbency the university will make steady progress toward the educational and research objectives that have guided it since its founding. These have taken on a new timeliness as interpreted by Dr. Bronk and we are determined to accomplish their substantial fulfillment. . . . In view of Dr. Reed's long and fruitful service to the university, the trustees are particularly grateful for his willingness to assume these further responsibilities at a time when he might rightfully expect to be free of heavy administrative duties."

MASSACHUSETTS

Crippled Children's Clinics.—Consultation clinics for crippled children have been scheduled for Greenfield, Aug. 6, Dr. Charles L. Sturdevant, Boston; Lowell, Aug. 14, Dr. Albert H. Brewster, Boston; and Fall River, Aug. 24, Dr. David S. Grice, Boston.

Alvarenga Prize to Dr. Moore.—On July 14 the College of Physicians of Philadelphia awarded the Alvarenga prize for 1953 to Dr. Francis D. Moore, surgeon-in-chief, Peter Bent Brigham Hospital, Boston, and Mosely Professor of Surgery, Harvard Medical School, Boston, for his outstanding contributions to the knowledge of the changes in body metabolism following surgery. The Alvarenga prize was established by the will of DaCosta Alvarenga of Lisbon, Portugal, an associate fellow of the College of Physicians of Philadelphia, to be awarded annually by the college on the anniversary of his death, July 14, 1883.

MICHIGAN

Fluoride Treatments for Children.—In a special program carried on by the public health dentistry section of the Michigan Department of Health in cooperation with local dentists and health, school, and civic groups, between 16,000 and 17,000 Michigan children, aged 3 to 13 years, are receiving fluoride treatments this summer to prevent tooth decay. The treatments will be given in 116 locations in 27 counties to rural children and to those in areas that do not have fluoride programs during the school year.

Medical Director Appointed.—Dr. James N. Dewane, Menominee, has been named medical director of Libby, McNeill & Libby, food canners, Chicago, to succeed Dr. Roscoe C. Eaton, who retired under the company's pension plan after 38 years' service. Dr. Dewane was previously affiliated with St. Agnes Hospital, Fond du Lac, Wis., and Newton D. Baker General Hospital, Martinsburg, W. Va. He spent two years in military service, attained the rank of captain, and was regimental surgeon of the 11th Constabulary Regiment.

Society News.—The Academy of Surgery of Detroit has elected Dr. Conrad R. Lam, president, Dr. Earl G. Merritt, president-elect, and Dr. Howard T. Howlett, secretary-treasurer. Dr. Roland P. Reynolds, retiring president, was chosen to fill a four year term as councilor.——At the annual meeting of the Detroit Dermatological Society, May 13, Dr. Henry A. Brunsting, Toledo, Ohio, was elected president, Dr. Charles J. Courville, Detroit, president-elect, Dr. Coleman Mopper, Detroit, secretary-treasurer, and Dr. Roy H. Holmes, Muskegon, recorder.

University News.—The University of Michigan Medical School, Ann Arbor, has announced the promotion to full professorship of Drs. A. James French (pathology) and John F. Holt (radiology). Dr. James W. Rae Jr., who has been acting chairman of the medical school's department of physical medicine and rehabilitation, has been named chairman and promoted to associate professor. Dr. Fred M. Davenport has been promoted to associate professorship in the department of internal medicine, school of public health. Also promoted to the rank of associate professor were Drs. Ivan F. Duff and Muriel C. Meyers (internal medicine); Herbert E. Sloan Jr. (surgery); Arthur L. Drew Jr. and Martha R. Westerberg (neurology); Lauren A. Woods (pharmacology); and Robert J. M. Horton (epidemiology). These physicians were promoted to the rank of assistant professor: Drs. Murray R. Abell (pathology), Samuel Behrman (obstetrics and gynecology), Melvin M. Figley (radiology), Everett R. Harrell Jr. (dermatology and syphilology), Willard J. Hendrickson (psychiatry), Robert C. Hendrix (pathology), Robert G. Lovell (internal medicine), and Aaron M. Stern (pediatrics and communicable diseases).

MISSISSIPPI

State Medical Election.—At the annual meeting in Biloxi the Mississippi State Medical Association elected Dr. Monterville Q. Ewing, Amory, president, Dr. Cummings H. McCall, Gulfport, president-elect, Drs. William T. Wilkins, Clarksdale, J. Harvey Johnston Jr., Jackson, and Richard H. Clark, Hattiesburg, vice-presidents, Dr. David S. Pankratz, University, historian, and Dr. Louie T. Carl, Jackson, associate editor.

MISSOURI

Hospital News.—At its annual meeting in St. Louis the St. Mary's Group of Hospitals Alumni elected the following St. Louis physicians as officers: Dr. J. Grey Jones, president; Dr. Carl J. Dreyer, vice-president; Dr. Malcolm B. Bawell, secretary; and Dr. Louis Keller, treasurer.

Personal.—Dr. Norman Tobias, St. Louis, recently addressed a joint meeting of the Buchanan County Medical and Dental Societies at St. Joseph on "Common Diseases of the Mouth." ——Dr. Robert Dean Woolsey, instructor in surgery, St. Louis University School of Medicine, conducted clinics in neurosurgery at the University of Turkey in Istanbul in June. His wife, Dr. Doris L. Woolsey, associate in clinical otolaryngology at Washington University School of Medicine, conducted clinics in otolaryngology at the university.——Dr. John R. Beem, St. Louis, has been appointed staff physician in the medical division of Sharp & Dohme, Philadelphia. Dr. Beem, who left the Army with the rank of captain in 1948, has since been affiliated with the Washington University School of Medicine, St. Louis.

Course in Medicine and Surgery.—The Greene County Medical Society will sponsor a postgraduate course in medicine and surgery, which will be presented by the department of postgraduate medical education of the University of Kansas School of Medicine. The course is planned for afternoon and evening sessions (2½ hours each) the last Wednesday of each month for a six month period beginning in October. It is open to anyone holding the degree of doctor of medicine. A registration fee of $25 is required for the course or $5 for each program (afternoon and evening). At the close of the course a certificate will be issued showing credit for the total hours attended. The tentative schedule of the programs, which will be offered in Springfield, includes a cardiovascular disease seminar and sessions on child psychiatry, hematology, ophthalmology, otolaryngology, chest diseases, medical emergencies, neurosurgery, and plastic surgery.

NEW JERSEY

Newark Honors Dr. Martland.—In recognition of his more than 40 years of outstanding professional service, the Newark City Commission will name the proposed new city hospital in honor of Dr. Harrison S. Martland, Newark, chief medical examiner of Essex County. Dr. Martland, who is professor of forensic medicine at New York University College of Medicine, became pathologist at Newark City Hospital in 1909. He is the holder of the Dr. Edward J. Ill Medal awarded by the Northern New Jersey Academy of Medicine.

NEW YORK

Name Director of Berg Institute.—L. Royal Christensen, Ph.D., assistant professor of microbiology at the New York University College of Medicine, has been appointed director of the new Henry W. and Albert A. Berg Institute for Experimental Physiology, Surgery and Pathology. He has been on the faculty of the college since 1941. The Berg institute was made possible through gifts from the late Dr. Albert A. Berg, who "contemplated a workshop where physiology and pathology would contribute nutriment for the growth of surgery" and whose will provided $500,000 for construction and a fund of well over one million dollars for maintenance of the institute named for him and his brother, the late Dr. Henry W. Berg.

Dr. Larimore Named Deputy Health Commissioner.—Dr. Herman E. Hilleboe, Albany, state health commissioner, has announced the appointment of Dr. Granville W. Larimore, Albany, as deputy health commissioner to succeed Dr. Hollis S. Ingraham, Albany, who was recently appointed first deputy commissioner. Dr. Larimore, who has been director of the Office of Public Health Education, New York State Department of Health, since 1947, is assistant professor of public health and preventive medicine at Albany Medical College and visiting lecturer at Columbia University School of Public Health. He was formerly educational director of the American Cancer Society. During World War II he served in the U. S. Army Medical Corps in which, as chief of the Health Education Unit in the Army Surgeon General's office, he was responsible for the development and administration of the health education program of the Army. He was awarded both the Army Commendation Medal and the Army Legion of Merit. Dr. Larimore was previously affiliated with the Municipal Contagious Disease Hospital in Chicago and served as assistant section chief in the contagious hospitals section of the Chicago Health Department. Since 1947 he has been consultant in public health education to the U. S. Army Surgeon General.

New York City

Dr. Hinsey to Direct Medical Center.—Joseph C. Hinsey, Ph.D., dean of Cornell University Medical College, has been appointed director of the New York Hospital-Cornell Medical Center to succeed Dr. Stanhope Bayne-Jones, for the past six years president of the joint administrative board of the center, who retired June 30 to become civilian technical director of research of the Army Medical Research and Development Program. Dr. Hinsey, who was also professor of anatomy at Cornell, has been affiliated with Washington University School of Medicine, St. Louis, Northwestern University Medical School, Chicago, and Stanford University School of Medicine, San Francisco. During World War II he served as consultant to the Committee on Neurosurgery of the National Research Council and directed research dealing with nerve injuries and with crash injuries in military airplane accidents. Dr. Hinsey, a past president of the Association of American Medical Colleges, has been chairman of its executive council since 1947. He is a trustee of the Sloan-Kettering Institute and the China Medical Board and a member of the Board of Managers of the Memorial Hospital. Since 1942 he has been a faculty representative on the board of trustees of Cornell University and is associate dean of the Graduate School. Dr. Hinsey served on the Committee on the Survey of Medical Education, which was jointly sponsored by the American Medical Association and the Association of American Medical Colleges in 1948-1953, and as a commissioner on the President's Commission on the Health Needs of the Nation in 1952. He is presently national president of Nu Sigma Nu medical fraternity.

Rockefeller Institute Elects New Officers.—At a special meeting of the board of trustees of the Rockefeller Institute for Medical Research, Detlev W. Bronk, Ph.D., president of Johns Hopkins University, Baltimore, and long a member of the board of scientific directors of the institute, was elected president and, in accordance with the newly revised bylaws, chief executive officer. Dr. Thomas M. Rivers, who was elected a vice-president and director, will assume the executive responsibility for an interim period while Dr. Bronk continues as president of Johns Hopkins. Dr. Rivers, who becomes the third director of the institute since its founding in 1901 under the directorship of Dr. Simon Flexner, succeeds Dr. Herbert S. Gasser (*J. A. M. A.* **152:**1154 [July 18] 1953). Mr. David Rockefeller, Ph.D., formerly president of the institute, was elected to the newly created post of chairman of the combined board, which resulted from a merger of the board of trustees and the board of scientific directors, and Dr. George H. Whipple, Rochester, N. Y., formerly vice-president, was elected vice-chairman of the board. The position of president of the board of scientific directors has been discontinued. Dr. Bronk, who was for 19 years director of the Eldridge Reeves Johnson Foundation for Medical Physics at the University of Pennsylvania, Philadelphia, served as coordinator of research during World War II for the air surgeon of the Army Air Forces and since then has been chairman of the National Research Council and president of the National Academy of Sciences. Dr. Rivers served on three commissions to study acute respiratory diseases in World War I and during World War II was on active duty in the medical corps of the U. S. Naval Reserve, being promoted to commodore in October, 1945. He was in charge of a naval research unit at the Rockefeller Institute Hospital and was the officer in command of Naval Medical Research Unit No. 2, which was stationed on Guam.

OHIO

Society News.—At the annual meeting of the board of directors of the Academy of Medicine of Cleveland, Dr. John H. Budd was elected president and Dr. George L. Sackett, vice-president. Dr. George R. Krause was reappointed secretary-treasurer.

Esophageal Speech Institute.—An institute on teaching and improving esophageal speech will be held Aug. 10 at the Cleveland Hearing and Speech Center, 11206 Euclid Ave., under the sponsorship of the American Cancer Society, National Cancer Institute of Institutes of Health, Office of Vocational Rehabilitation, Cleveland Otolaryngological Society, Cleveland Academy of Medicine, and the Western Reserve University School of Medicine. Surgeons, speech pathologists, and lay persons are invited to attend the sessions. Nonspeaking persons who have had a laryngectomy may attend without charge and may be sent by surgeons, cancer societies, societies for crippled persons, and rehabilitation services.

OREGON

University News.—The Tektronic Foundation of Portland has contributed $26,800 to support the surgery department's pain project and other research programs at the University of Oregon, Portland; $16,000 will be used for the two year salary of a neurophysiologist to work under the direction of Dr. William K. Livingston, head of the surgery department, and $10,800 to support graduate assistants for the next three years who will participate in research headed by John M. Brookhart, Ph.D., head of the physiology department.——Dr. Paul G. Hafner, director of the crippled children's program at the University of Oregon Medical School, Portland, since September, 1946, has resigned to devote full time to the private practice of orthopedic surgery in Vancouver, Wash., where he will be associated with Dr. Joseph H. Gill. Dr. Richard L. Sleeter, Medford, has been named to replace Dr. Hafner, with the rank of assistant professor of pediatrics. Other faculty appointments include Dr. Robert E. Buckmaster, clinical instructor in orthopedic surgery; Dr. Robert E. Rinehart, Wheeler, visiting clinical instructor in medicine; and Dr. Nathaniel D. Wilson, clinical instructor in surgery.——A Fulbright research scholarship to travel and study for six months in Italy has been awarded Dr. Robert S. Dow, associate clinical professor of medicine, University of Oregon Medical School, Portland. He will continue his work on neurophysiological research at the University of Pisa.

SOUTH DAKOTA

Fifty Year Club.—Fifty Year Club pins were recently awarded to Drs. John L. Chassell, Belle Fourche, Arthur S. Jackson, Rapid City, and Theodore F. Riggs, Pierre.

State Medical Election.—At the annual meeting in Rapid City the South Dakota State Medical Association elected Dr. Roland G. Mayer, Aberdeen, president; Dr. Arthur W. Spiry, Mobridge, president-elect; Dr. F. Daniels Gillis, Mitchell, vice-president; and Dr. Geoffrey Cottam, Sioux Falls, secretary-treasurer.

Personal.—Dr. Rezin Reagan, Sioux Falls, has retired after 40 years of practice. His four children, however, continue in medical fields: Dr. Paul C. Reagan will carry on his father's practice; Dr. James L. Reagan is in his first year of internship at Western Pennsylvania Hospital, Pittsburgh; Charles Reagan is an executive director with the U. S. Public Health Service in Spokane, Wash.; and the daughter, Genevieve, is an anesthetist at Sioux Valley Hospital, Sioux Falls. Dr. Reagan has been medical director for the National Reserve Life Insurance Company of Sioux Falls and Topeka, Kan., for 30 years.

TENNESSEE

Society News.—The Tennessee Academy of Preventive Medicine and Public Health, which held its first annual meeting May 20 in Nashville, announces that annual sessions hereafter will be held in conjunction with the annual meeting of the Tennessee State Medical Association. Membership in the academy is limited to diplomates of the American Board of Preventive Medicine resident in Tennessee. Officers of the academy are: Dr. Robert H. Hutcheson, Nashville, president; Dr. Monroe F. Brown, Nashville, vice-president; Dr. John J. Lentz, Nashville, president-elect; and Dr. Paul M. Golley, Chattanooga, secretary-treasurer.

WEST VIRGINIA

Cardiac Problems in Industry.—The Golden Clinic-Memorial General Hospital Association at Elkins will hold a symposium Sept. 7-8, on "The Heart in Industry." The medical panel will be comprised of the following physicians: Dr. W. Frederick Richmond, Beckley, president, West Virginia Heart Association; Dr. Robert P. Glover, president, American College of Cardiology, and clinical professor of thoracic surgery, Hahnemann Medical College and Hospital of Philadelphia; Dr. Donald S. Smith, consulting cardiologist, Fisher Body Division, Pontiac, Mich.; Dr. Edward M. Kline, Cleveland, medical consultant, General Electric Company and member of the Committee on the Cardiac in Industry of the AHA; and Dr. Leonard J. Goldwater, chairman, American Heart Association's Committee on the Cardiac in Industry and professor of occupational medicine, Columbia University School of Public Health, New York. Major labor groups and personnel divisions of industry have been invited to participate. The symposium is open to the medical profession and those directly interested in the rehabilitation problem. Further information may be obtained from Dr. Harold L. Jellinek, Golden Clinic, Elkins.

WISCONSIN

Course in Obstetrics.—The University of Wisconsin Medical School, Madison, will hold a postgraduate course in obstetrics, Sept. 1-3 in the graduate lecture room (426 State of Wisconsin General Hospital). This course, conducted by Dr. John W. Harris, professor of obstetrics and gynecology, will have as guest faculty member Dr. Curtis J. Lund, professor and chairman of the department of obstetrics and gynecology, Rochester (N. Y.) University School of Medicine. Advance registration (limited to 40 registrants) is required; fee, $20. Application for registration should be addressed to Dr. Robert C. Parkin, Coordinator of Graduate Medical Education, University of Wisconsin Medical School, 418 N. Randall Ave., Madison 6.

GENERAL

Vitamin Foundation Grants.—Fourteen new grants to 12 universities and 2 hospitals, for research on vitamins and nutrition, amounting to $69,710, have been announced by Dr. Robert S. Goodhart, scientific director of the National Vitamin Foundation, Inc., New York. These grants bring the total appropriated for research by the foundation since its incorporation in February, 1946, to $704,890.50. The foundation has appropriated more than $135,000 in additional funds for educational and public health purposes.

WHO Publishes Epidemic-Warning Cable Code.—The World Health Organization has announced in Geneva the publication of the first cable code to be used on a world-wide scale for transmitting information on epidemics and quarantine measures. The code will be used, beginning Dec. 1, in WHO's epidemic-intelligence service through which the agency is notified of outbreaks of certain diseases and then broadcasts the information to health authorities. Use of CODEPID, the WHO epidemiological cable code, is said to be restricted to national health authorities and WHO offices.

National Medical Fellowships.—Dr. Nathaniel O. Calloway, Chicago, vice-president of National Medical Fellowships, Inc., and Dr. Franklin C. McLean, Chicago, secretary-treasurer, announce the awarding of $74,075 to 46 Negro physicians and scholars in the medical and related fields for the year 1953-1954. National Medical Fellowships, Inc., formerly Provident Medical Associates, which was organized at the end of World War II, has awarded a total of $337,958 in grants to 146 persons for "improvement of Negro medical practice through the advancement of education and research."

Chronic Illness Planning.—The Commission on Chronic Illness has issued a 48 page mimeographed publication entitled "Welfare Council Activities in Chronic Illness Planning." The report, a summary of information that the commission obtained several years ago from a questionnaire to 124 community welfare councils, describes the efforts of community welfare councils in 70 cities and towns to make plans for

meeting the needs created by chronic illness in their communities and gives a detailed discussion of the various methods used for local studies of prevalence and adequacy of facilities. A limited number of copies are available and may be obtained, free of charge, from the commission offices at 615 N. Wolfe St., Baltimore 5.

Theobald Smith Award.—The Theobald Smith Award of $1,000 and a bronze medal, sponsored by Eli Lilly and Company of Indianapolis under the auspices of the American Association for the Advancement of Science, will be given for the ninth time at the Boston meeting in December. The prize is given for "demonstrated research in the field of the medical sciences, taking into consideration independence of thought and originality." Nominations should be sent to Dr. Allan D. Bass, Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, Tenn., before Sept. 15. They should be in triplicate and accompanied by full information concerning the nominee's personality, training, and research work. United States citizens under 35 years of age on Jan. 1, 1953, are eligible.

New Trudeau Societies.—According to the National Tuberculosis Association, three new state Trudeau societies were organized during the fiscal year 1952-1953, bringing to 28 the number of states having medical sections in their state tuberculosis associations. The new societies and their officers are: Nebraska Trudeau Society—Dr. William E. Nutzman, Kearney, president; Dr. Herbert B. Kennedy, Omaha, vice-president; Dr. Stanley E. Potter, Omaha, secretary-treasurer. Oklahoma Trudeau Society—Dr. Richard M. Burke, Oklahoma City, president; Dr. Robert M. Shepard, Tulsa, vice-president; Dr. Mark D. Holcomb, Enid, secretary-treasurer. West Virginia Trudeau Society—Dr. William L. Cooke, Charleston, president; Dr. Hugh S. Edwards, Beckley, secretary-treasurer.

Association of University Anesthetists.—Announcement has been made of the formation of the Association of University Anesthetists. The organization committee included physician anesthetists from the following universities and colleges: Columbia, Harvard, Minnesota, Pennsylvania, Tufts, Vanderbilt, and Wisconsin. Additional anesthetists have been elected from the following medical schools: Albany, Boston, Cornell, Duke, Georgia, Johns Hopkins, New York, New York State, Oregon, Rochester, Texas, Tulane, Washington, Wayne, and Yale. The purpose of the new group is to advance the art and science of anesthesia by encouraging original investigations, by developing methods of teaching, and by such free and informal interchange of ideas as a limited membership and common aims make possible.

Fellowships for Psychiatrists.—The National Foundation for Infantile Paralysis has a number of fellowships available to psychiatrists interested in emotional problems of the physically disabled. Eligibility requirements include two years of graduate training in psychiatry. Financial benefits are based on individual needs. Appointments will be made for one year, subject to renewal. The programs of the fellows should be undertaken in a center concerned with rehabilitation of the physically disabled that has affiliations with an approved department of psychiatry and affords opportunity for work with poliomyelitis patients with respiratory difficulties. The department of psychiatry is to be responsible for supervision and training of the fellows. Information may be obtained from the Division of Professional Education, National Foundation for Infantile Paralysis, 120 Broadway, New York 5.

Jane Coffin Childs Memorial Fund.—The Jane Coffin Childs Memorial Fund for Medical Research has announced that between Oct. 25, 1952, and May 15, 1953, it appropriated $238,480 for support of cancer research projects and fellowships. Of the 19 grants, the largest were: (1) to Dr. Francisco Duran-Reynals, lecturer, department of microbiology, Yale University School of Medicine, New Haven, Conn., $49,500 for the study of the part played by viruses in the genesis of cancer; (2) to Dr. Harris Busch, assistant professor of physiological chemistry, Yale University School of Medicine, New Haven, Conn., $25,950 for investigations on the metabolism of tumors in vivo; (3) to Dr. William W. Winternitz, instructor, and Dr. Cyril N. H. Long, professor, department of physiology, Yale University School of Medicine, $24,000 for investigations on the effect of transplantable tumors on the metabolism of the host (albino rats); and (4) to Dr. Baldwin H. Lucke, professor of pathology, University of Pennsylvania Medical School, Philadelphia, $23,100 for investigations on enzyme patterns in relation to the development and growth of neoplasms and the mechanism of metastasis.

Van Meter Prize Award.—The American Goiter Association offers the Van Meter prize award of $300 and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The award will be made at the annual meeting of the association in Boston, April 29 to May 1, 1954, if essays of sufficient merit are presented in competition. A place will be reserved on the program for the presentation of the prize award essay by the author, and the essay will be published in the annual proceedings of the association. Essays may cover either clinical or research investigations, should not exceed 3,000 words, and must be presented in English. A typewritten, double-spaced copy in duplicate should be sent to the Corresponding Secretary, Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., not later than Jan. 15, 1954.

Cardiac Research Applications.—Dr. Irving S. Wright, New York, chairman of the scientific council, American Heart Association, announces that applications are now being accepted for research awards to be made during the coming year under the joint auspices of the association and its affiliates throughout the country. Applications for research fellowships and established investigatorships should be filed by Sept. 15 and applications for research grants-in-aid no later than Dec. 1. Information and forms may be obtained from the Medical Director, American Heart Association, 44 E. 23rd St., New York 10. The research awards will be available for studies to be conducted during the year beginning July 1, 1954. Established investigatorships ($6,000 to $9,000), which may be extended annually for a five year period, are available to scientists of proven ability who are engaged in a research career. Research fellowships ($3,500 to $5,500), awarded for a one year period, are open to persons interested in research and in an academic career. Grants-in-aid, awarded in varying amounts usually not exceeding $10,000, are made on the basis of specific acceptable projects to experienced investigators working in nonprofit institutions, medical schools, hospitals, and laboratories, who have demonstrated their productiveness or who otherwise give promise of accumulating useful new information.

Lasker Awards in Planned Parenthood.—The annual Albert and Mary Lasker Foundation awards in planned parenthood were recently bestowed on the following three persons. 1. Dr. Herbert Thoms, chairman of the department of obstetrics and gynecology, Yale University School of Medicine, New Haven, Conn., received the award "in recognition of his contribution to marital health and happiness in the related fields of obstetrics, marriage counseling, and treatment for infertility." Dr. Thoms, who pioneered in research and development of methods of natural childbirth and rooming-in for mother and child, founded the first infertility clinic in Connecticut and was a prime mover in organizing the first marriage counseling clinic (at Yale) under medical school auspices. 2. Dr. John William Norton, Raleigh, N. C., state health officer of North Carolina, was given an award "for his far-sighted and energetic leadership in making effective an integrated birth control program in the public health services of North Carolina." Dr. Norton is said to have been a leader in the movement establishing in 1937 the first state-supported birth control clinics in the United States and later guiding the integration of planned parenthood into the program of local health department service in the state's 100 counties. 3. Mrs. Philip W. Pillsbury, immediate past president of the Planned Parenthood Federa-

tion, Inc., and now its first vice-president and Executive Committee chairman, received the award "for her unique contribution to the well-being of American family life in our generation."

Society News.—At the annual meeting in New York the Medical Society's Executives Conference elected Mr. Ralph W. Neill, Seattle, executive secretary of the Washington State Medical Society, president; Mr. Charles Lively, Charleston, W. Va., executive secretary of the West Virginia State Medical Association, president-elect; and Mr. William H. Bartleson, Kansas City, Mo., executive secretary of the Jackson County (Mo.) Medical Society, secretary-treasurer.——The American Congress of Physical Medicine and Rehabilitation has appointed a committee for the coordination and integration of physical medicine and rehabilitation in geriatrics, with Michael M. Dacso, New York, as chairman, and Nila G. Kirkpatrick Covalt, Rocky Hill, Conn., Harold Dinken, Denver, Karl Harpuder, New York, and G. Morris Piersol, Philadelphia, as members.——At the annual meeting in Hot Springs, Va., the American Orthopaedic Association elected Dr. Alfred R. Shands Jr., Wilmington, Del., president; Dr. Leo S. Lucas, Portland, Ore., vice-president; Dr. J. Warren White, Honolulu, Hawaii, president-elect; Dr. George O. Eaton, Baltimore, secretary; and Dr. H. Page Mauck, Richmond, Va., treasurer. ——At its annual meeting at the Sheraton-Mount Royal Hotel, Montreal, Canada, May 3-5, 1954, the American Association for Thoracic Surgery will initiate a thoracic surgical forum for the presentation of short papers on current thoracic research, anatomy, and modified surgical techniques. Papers at this session will be limited to 10 minutes (including the showing of lantern slides or other illustrative material) with 3 minutes maximum for the discussion of each paper. Abstracts (200 to 250 words) for the presentation of all papers at the 1954 meeting must be received on or before Jan. 1 and should be labeled "For Forum" or "For Regular Program." Five copies of each abstract should be sent to the secretary of the association, Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif.

Dietetic Association Meets in Los Angeles.—The American Dietetic Association will hold its annual meeting at the Shrine Auditorium and Convention Hall, Los Angeles, Aug. 25-28. Dr. James R. Wilson, Secretary, A. M. A. Council on Foods and Nutrition, will report on "Low Sodium Foods and Diets" as part of a program on "Newer Findings in Diet Therapy," which will include "The Intake of Excess Fat and Calories in Relation to the Development of Human Atherosclerosis" by Dr. John W. Gofman, Berkeley, Calif., and "Comparative Effects of Diets Containing Large Amounts of Animal and Vegetable Fat Respectively, upon Serum Lipids in Normal and Abnormal Human Subjects" by Dr. Laurance W. Kinsell, Oakland, Calif. Participating in presentations on "Recent Research" will be Drs. Garnett Cheney, San Francisco ("The Present Status of Vitamin U Therapy in the Dietary Treatment of Peptic Ulcer") and Horace R. Getz, Altadena, Calif. ("What Are the Problems in Feeding the Tuberculous Patient?"). In a public relations program Tuesday evening Dr. Eugene Pumpian-Mindlin, Los Angeles, will have as his topic "If You Please." On Wednesday Dr. Wilton L. Halverson, San Francisco, will present "Bilateral Health Programs in Latin America" as the opening topic for a panel on "Steps Toward Better World Nutrition." Dr. James A. Halsted, Los Angeles, will present the physician's viewpoint in a panel on "Cooperative Approach Aids Medical Therapy" Thursday, 1 p. m., and Dr. Anthony J. Rourke, New York, will discuss teamwork during a panel on "Challenges to You," 2 p. m. Other presentations by physicians include:

Emotional Factors in Child Feeding, John A. Anderson, San Francisco.
The Obesity Problem, Harold I. Harvey, Berkeley.
Newer Concepts in the Treatment of the Diabetic, Samuel Soskin, Los Angeles.
Revisions of the Recommended Daily Dietary Allowances, Robert E. Shank, St. Louis.
Psychological Aspects of Food Faddism, Solon D. Samuels, Los Angeles.

At the annual banquet in the Hotel Statler, Friday, 7 p. m., Dr. Frank R. Bradley, St. Louis, will present the Marjorie Hulsizer Copher award for 1953.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions in the weeks ended as indicated:

Area	July 25, 1953: Paralytic Type	July 25, 1953: Total Cases Reported	July 26, 1952 Total
New England States			
Maine	10	17	3
New Hampshire	..	4	1
Vermont	1	1	2
Massachusetts	10	22	8
Rhode Island	2	5	..
Connecticut	1	15	15
Middle Atlantic States			
New York	16	81	76
New Jersey	18	28	10
Pennsylvania	..	26	24
East North Central States			
Ohio	17	88	179
Indiana	..	14	34
Illinois	22	76	68
Michigan	15	84	79
Wisconsin	..	16	33
West North Central States			
Minnesota	34	78	38
Iowa	5	25	116
Missouri	15	39	33
North Dakota	2	4	1
South Dakota	..	9	15
Nebraska	8	10	72
Kansas	..	22	24
South Atlantic States			
Delaware	..	3	3
Maryland	9	22	3
District of Columbia	..	2	..
Virginia	20	51	15
West Virginia	9	26	32
North Carolina	23	87	15
South Carolina	4	11	7
Georgia	6	28	18
Florida	7	20	20
East South Central States			
Kentucky	3	17	51
Tennessee	11	51	15
Alabama	16	21	12
Mississippi	..	14	54
West South Central States			
Arkansas	8	12	16
Louisiana	9	31	39
Oklahoma	11	39	66
Texas	21	86	259
Mountain States			
Montana	2	5	8
Idaho	..	1	16
Wyoming	1	5	2
Colorado	2	9	31
New Mexico	..	2	22
Arizona	7	22	7
Utah	..	5	6
Nevada	..	1	..
Pacific States			
Washington	..	17	36
Oregon	3	5	14
California	46	95	75
Territories and Possessions			
Alaska	5	9	..
Hawaii	..	1	10
Puerto Rico	3	3	1
Total	402	1,365	1,684

LATIN AMERICA

Goiter Survey in El Salvador.—A survey, recently reported, indicates that endemic goiter in school children constitutes a serious public health problem in El Salvador. Based on the examination of nearly 35,000 school children in urban and rural areas, it revealed that 22.8% of 26,400 children outside the capital city had enlarged thyroids. In the capital the incidence was 1.1% for 8,000 children. Glands were considered enlarged if on palpation they were found to be four to five times their "normal" size. Of the total number of goiters, 6.2% were of the clearly visible type. The average iodine content of the salt was 0.22 parts of iodine per 10,000 parts of salt, whereas the recommended ratio for prevention of endemic goiter under ordinary circumstances is 1 part iodine per 10,000 parts salt.

FOREIGN

Course on Allergic Diseases.—A course on allergic diseases, including both theoretical instruction and practical work, will be given Oct. 19-23 at the Propaedeutic Medical Clinic of the Hôpital Broussais, under the direction of Prof. Pasteur Vallery-Radot. The course will include anaphylaxis and allergy; experimental anaphylaxis; respiratory allergy; alimentary allergy; cutaneous allergy; digestive, renal, cardiovascular, and hematological manifestations of allergy; allergy to physical agents; antihistamines; and treatment of allergic conditions. Since enrollment is limited, requests for registration should be addressed promptly to the Propaedeutic Medical Clinic of the Hôpital Broussais, 96, rue Didot, Paris XIVe.

Seminar in Health Education.—The Central Council for Health Education in England will conduct its annual residential summer school in health education at Royal Holloway College, Surrey, just outside of London, Aug. 10-20, for professional workers in medical, educational, industrial, and welfare services. The program is organized on a group discussion basis, and a social program is also provided. The inclusive fee for tuition and residence is £16 16s. (about $47). Information may be secured from the Medical Director, Central Council for Health Education, Tavistock House, Tavistock Square, London, W.C.1.

CORRECTION

Medical Education Foundation.—The editorial "Medical Education Foundation Reports Progress," which appeared in THE JOURNAL July 11, 1953, page 1044, listed Connecticut among the eight leading states in foundation activity. The eight leading states should read in order as follows: Nebraska, Indiana, South Dakota, Vermont, Wyoming, New Hampshire, Colorado, and Delaware.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1953 Clinical Session, St. Louis, Dec. 1-4.
1954 Annual Session, San Francisco, June 21-25.
1954 Clinical Session, Miami, Florida, Nov. 30-Dec. 3.
1955 Annual Session, Atlantic City, N. J., June 6-10.
1955 Clinical Session, Boston, Nov. 29-Dec. 2.

NATIONAL CONFERENCE ON PHYSICIANS AND SCHOOLS, Moraine-on-the-Lake Hotel, Highland Park, Ill., Sept. 30-Oct. 2. Dr. W. W. Bauer, 535 N. Dearborn St., Chicago 10, Director.

PUBLIC RELATIONS INSTITUTE, Drake Hotel, Chicago, Sept. 2-3. Mr. Leo E. Brown, 535 North Dearborn St., Chicago 10, Director.

AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. William F. Mengert, 2211 Oak Lawn Ave., Dallas, Texas, Secretary.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA, Drake Hotel, Chicago, Oct. 1-3. Dr. James K. Stack, 700 North Michigan Blvd., Chicago, Secretary.

AMERICAN CONGRESS OF PHYSICAL MEDICINE, Palmer House, Chicago, Aug. 31-Sept. 4. Dr. Walter J. Zeiter, 30 North Michigan Ave., Chicago 2, Executive Director.

AMERICAN DIETETIC ASSOCIATION, Los Angeles, Aug. 24-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY, Commander and Continental Hotels, Cambridge, Mass., Aug. 17-22. Dr. John A. Abbott, Massachusetts General Hospital, Boston 14, Secretary.

AMERICAN HOSPITAL ASSOCIATION, San Francisco, Aug. 31-Sept. 3. Mr. George Bugbee, 18 East Division St., Chicago 11, Executive Director.

AMERICAN MEDICAL WRITERS' ASSOCIATION, Elk's Club, Springfield, Ill., Sept. 23. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

AMERICAN ROENTGEN RAY SOCIETY, Netherland Plaza, Cincinnati, Sept. 29-Oct. 2. Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Secretary.

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Fall Meeting, Yale University, New Haven, Conn., Sept. 7-9. Dr. Carl C. Pfeiffer, 1853 West Polk St., Chicago 12, Secretary.

BIOLOGICAL PHOTOGRAPHIC ASSOCIATION, Hotel Statler, Los Angeles, Aug. 31-Sept. 3. Miss Jane H. Waters, 533 West 57th St., New York 19, Secretary.

COLORADO STATE MEDICAL SOCIETY, Savoy Hotel, Denver, Sept. 29-Oct. 2. Mr. Harvey T. Stethman, 835 Republic Bldg., Denver 2, Executive Secretary.

GERONTOLOGICAL SOCIETY, Mark Hopkins Hotel, San Francisco, Aug. 25-27. Dr. Nathan W. Shock, Baltimore City Hospitals, Baltimore 24, Secretary.

GULF COAST CONFERENCE ON INDUSTRIAL HEALTH, Shamrock Hotel, Houston, Tex., Oct. 1-3. Dr. Sidney Schnur, 411 Medical Arts Bldg., Houston 2, Tex., Vice Chairman.

KANSAS CITY SOUTHWEST CLINICAL SOCIETY, Kansas City, Mo., Sept. 28-Oct. 1. Dr. W. H. Algie, 825 North 7th Street, Kansas City, Kans., Secretary.

KENTUCKY STATE MEDICAL ASSOCIATION, Brown Hotel, Louisville, Sept. 22-24. Dr. Bruce Underwood, 620 South Third St., Louisville 2, Secretary.

MICHIGAN STATE MEDICAL SOCIETY, Pantlind Hotel and Civic Auditorium, Grand Rapids, Sept. 23-25. Dr. L. Fernald Foster, 606 Townsend St., Lansing 15, Secretary.

MISSISSIPPI VALLEY MEDICAL SOCIETY, Springfield, Ill., Sept. 23-25. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

MONTANA MEDICAL ASSOCIATION, Northern Hotel, Billings, Sept. 17-20. Mr. L. R. Hegland, 104 North Broadway, Billings, Executive Secretary.

NATIONAL MEDICAL ASSOCIATION, Nashville, Tenn., Aug. 10-14. Dr. John T. Givens, 1108 Church St., Norfolk 10, Va., Executive Secretary.

NEUROSURGICAL SOCIETY OF AMERICA, The Broadmoor, Colorado Springs, Colo., Sept. 23-27. Dr. C. D. Hawkes, 22 North Manassas St., Memphis 5, Tenn., Secretary.

NEVADA STATE MEDICAL ASSOCIATION, Carter Hotel, Elko, Sept. 24-26. Dr. William A. O'Brien III, 505 Chestnut St., Reno, Secretary.

NORTHERN MINNESOTA MEDICAL ASSOCIATION, Fergus Falls, Aug. 28-29. Dr. C. L. Oppegaard, Crookston, Secretary.

NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Harrison, B. C., Sept. 18-19. Dr. Clarence C. Pearson, 1115 Terry Ave., Seattle 1, Wash., Secretary.

NORTH TEXAS-SOUTHERN OKLAHOMA FALL CLINICAL CONFERENCE, Wichita Falls, Texas, Sept. 16. Dr. C. H. Wilson, 1300 Eighth St., Wichita Falls, Texas, Secretary.

PENNSYLVANIA, MEDICAL SOCIETY OF THE STATE OF, William Penn Hotel, Pittsburgh, Sept. 21-24. Dr. Harold B. Gardner, 230 State St., Harrisburg, Secretary.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:
NORTH DAKOTA, Fargo, Sept. 12. Dr. Robert B. Radl, 221 Fifth St., Bismarck, Governor.
ARKANSAS-OKLAHOMA, Tulsa, Okla., Sept. 19. Dr. Wann Langston, 117 North Broadway, Oklahoma City 2, Governor.

SOCIETY OF AMERICAN BACTERIOLOGISTS, Palace Hotel, San Francisco, Aug. 10-14. Dr. John H. Bailey, Sterling-Winthrop Research Institute, Rensselaer, N. Y., Secretary.

SOUTHWESTERN SURGICAL CONGRESS, Hotel Utah, Salt Lake City, Sept. 21-23. Dr. C. R. Rountree, 1227 Classen St., Oklahoma City 3, Secretary.

TENNESSEE VALLEY MEDICAL ASSEMBLY, Read House Hotel, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, 612 Medical Arts Bldg., Chattanooga 3, President.

U. S. CHAPTER, INTERNATIONAL COLLEGE OF SURGEONS, Waldorf-Astoria, New York, Sept. 13-17. Dr. Karl Meyer, 1516 Lake Shore Drive, Chicago 10, Secretary.

UTAH STATE MEDICAL ASSOCIATION, Salt Lake City, Sept. 10-12. Dr. Homer E. Smith, 42 South Fifth East St., Salt Lake City 2, Secretary.

WASHINGTON STATE MEDICAL ASSOCIATION, Olympic Hotel, Seattle, Sept. 13-16. Dr. Bruce Zimmerman, 338 White-Henry-Stuart Bldg., Seattle 1, Secretary.

FOREIGN

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, Leeds, England, May 13-15, 1954. Dr. Henry W. S. Wright, 45 Lincoln's Inn Fields, London W.C.2, England, Honorary Secretary.

CANADIAN MEDICAL ASSOCIATION, Vancouver, B. C., Canada, June 18-22, 1954. Dr. T. C. Routley, 135 St. Clair Ave. W., Toronto 5, Ont., Canada, General Secretary.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Chateau Frontenac, Quebec, Canada, October 26-29. Dr. A. William Friend, 515 Nome Ave., Akron 20, Ohio, Chairman, Program Committee.

CONGRESS OF THE INTERNATIONAL ASSOCIATION OF LIMNOLOGY, Cambridge and Windermere, England, Aug. 20-30. For information write: Professor G. C. Hutchinson, Osborn Zoological Laboratory, Yale University, New Haven, Conn., U. S. A.

CONGRESS OF THE INTERNATIONAL LEAGUE AGAINST RHEUMATISM, Geneva, Switzerland and Aix-les-Bains, France, Aug. 23-29. For information write: Dr. W. Tegner, The London Hospital, London E.1, England.

CONGRESS OF THE INTERNATIONAL SOCIETY OF ANGIOLOGY, Lisbon, Portugal, Sept. 18-20. Dr. Henry Haimovici, 105 East 90th St., New York 28, N. Y., U. S. A., Secretary.

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 14-20. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

INTERIM MEETING, AERO MEDICAL ASSOCIATION, University of Brussels Medical School, Brussels, Belgium, Sept. 24-27. Dr. Andre Allard, Medical Director of SABENA, 145 Rue Royale, Brussels, Belgium, Secretary.

INTERNATIONAL CANCER CONGRESS, Sao Paulo, Brazil, July 23-29, 1954. Prof. A. Prudente, 171 rua Benjamin Constante, Sao Paulo, Brazil, President.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 15-19, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS OF ACUPUNCTURE, Kolpinghaus, Adolf-Kolping-Strasse 1, Munich, Germany, August 22-25. Dr. G. Bachmann, 29 Lilienstrasse, München 9, Germany, Organizer and Secretary.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF THE EUROPEAN SOCIETY OF HAEMATOLOGY, Amsterdam, Holland, Sept. 8-12. Dr. M. C. Verloop, Maliesingle 15, Utrecht, Holland, Secretary.

INTERNATIONAL CONGRESS ON GENETICS, Bellagio, Italy, August 24-31. Prof. C. Barigozzi, Instituto de Genetica, Universita de Milano, 10 via Celoria, Milan, Italy, Secretary.

INTERNATIONAL CONGRESS OF HIPPOCRATIC MEDICINE, Evian, France, Sept. 3-6. Prof. P. Delore, 13, rue Jarente, Lyon, France, Secretary-General.

INTERNATIONAL CONGRESS OF HYDROCLIMATISM AND THALASSOTHERAPY, Dubrovnik, Yugoslavia, May 8-16, 1954. Prof. C. Plavsic, Zeleni Venac 1, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Sao Paulo, Brazil, April 26-May 2, 1954. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U.S.A., Secretary-General.

INTERNATIONAL CONGRESS OF LOGOPEDICS AND PHONIATRICS, Zurich, Switzerland, Sept. 1-5. Dr. Deso A. Weiss, 115 East 86th St., New York 28, N. Y., U. S. A., General Secretary.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept 6-12. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS ON OBSTETRICS AND GYNECOLOGY, Geneva, Switzerland, July 26-31, 1954. Dr. H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland, President.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Havana, Cuba, Oct. 12-17. Prof. Felix Hurtado, 5a Avenue 124, Miramar, Havana, Cuba, President.

INTERNATIONAL CONGRESS OF PSYCHOLOGY, Montreal, Canada, June 7-12, 1954. For information write: Prof. H. S. Langfeld, International Union of Scientific Psychology, Eno Hall, Princeton University, Princeton, N. J., U. S. A.

INTERNATIONAL CONGRESS FOR PSYCHOTHERAPY, Zurich, Switzerland, July 21-24, 1954. Dr. H. K. Fierz, Theaterstrasse 12, Zurich 1, Switzerland, Secretary General.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyoglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL LEPROSY CONGRESS, Madrid, Spain, Oct. 3-10. Dr. Felix Contreras, Moreto 15, Madrid, Spain, Secretary.

INTERNATIONAL NEUROLOGICAL CONGRESS, LISBON, Portugal, Sept. 7-12. Prof. Almeida Lima, Avenida do Brazil 53, Lisbon, Portugal, Secretary-General.

INTERNATIONAL OFFICE OF DOCUMENTATION OF MILITARY MEDICINE, Rome, Italy, Oct. 14-18. Colonel Medecin Prof. A. Campana, Office of the Ministero della Difesa-Esercito, Rome, Italy, Secretary.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL SOCIETY FOR THE STUDY OF BIOLOGICAL RHYTHMS, Basle, Switzerland, Sept. 18-19. For information write: Prof. Dr. F. Georgi, Neurologische Universitats-Poliklinik, Socinstrasse 55, Basle, Switzerland.

INTERNATIONAL VETERINARY CONGRESS, Stockholm, Sweden, Aug. 9-15. Prof. Axel Isaksson, Institute of Veterinary Medicine, Stockholm 50, Sweden, Secretary.

JOURNEES MEDICALES, Paris, France, April 21-25, 1954. For information write: Secretariat of the Journees, 12, rue Pierre-Geofroix, Colombes (Seine) France.

LATIN AMERICAN CONGRESS OF OBSTETRICS AND GYNECOLOGY, Buenos Aires, Argentina, Oct. 26-31.

LATIN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY, Caracas, Venezuela, Feb. 21-25, 1954. Dr. Victorino Marquez Reveron, Centro Medico, Caracas, Venezuela, Secretary-General.

PACIFIC SCIENCE CONGRESS, Quezon City and Manila, Philippines, Nov. 16-28. Dr. Patrocinio Valenzuela, College of Pharmacy, University of the Philippines, Quezon City, Philippines, Secretary-General.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, Mexico, D.F., Mexico, Feb. 28-March 4, 1954.

PAN AMERICAN MEDICAL ASSOCIATION, International Medical Cruise Congress, S. S. Nieuw Amsterdam, Jan. 6-22, 1954. Dr. Joseph J. Eller, 745 Fifth Avenue, New York 22, N. Y., U. S. A., Executive Director.

PAN AMERICAN MEDICAL WOMEN'S ALLIANCE, Beekman Towers Hotel, New York, N. Y., Sept. 24-Oct. 1. Dr. Ina Marsh, 140 Linwood Ave., Buffalo, N. Y., U. S. A., Registration Chairman.

PERSIAN GULF MEDICAL SOCIETY, Dhahran, Saudi Arabia, Dec. 7-8. Dr. N. J. Conan Jr., Department of Internal Medicine, Arabian American Oil Company, Dhahran, Saudi Arabia, Secretary.

REGIONAL MEETING, AMERICAN COLLEGE OF PHYSICIANS, San Juan, Puerto Rico, Oct. 15-17. Dr. R. Rodriquez-Molina, Veterans Administration Center, San Juan, Puerto Rico, Governor.

SECTIONAL MEETING, AMERICAN COLLEGE OF SURGEONS, London, England, May 17-19, 1954. Dr. Michael L. Mason, 40 East Erie St., Chicago 11, Ill., U. S. A., Secretary.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 22-29. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICAL THERAPY, London, England, Sept. 7-12. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C.1, England, Secretary.

WORLD FEDERATION FOR MENTAL HEALTH, Vienna, Austria, Aug. 17-23. For information write: Miss E. M. Thornton, 19 Manchester St., London, W.1, England.

WORLD MEDICAL ASSOCIATION, The Hague, Netherlands, Aug. 31-Sept. 7. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., Secretary-General.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALASKA:* Anchorage and Juneau, Sept. 7. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

ARIZONA:* Phoenix, Oct. 24. Ex. Sec., Mr. Robert Carpenter, 541 Security Bldg., Phoenix.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Director of Medical Services, Guam Memorial Hospital, Agana.

MONTANA: Helena, Oct. 5. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEW HAMPSHIRE: Concord, Sept. 9. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW MEXICO:* Oct. 12-13, Santa Fe. Sec., R. C. Derbyshire, 227 E. Palace Ave., Sante Fe.

NORTH CAROLINA: *Reciprocity*. Asheville, Oct. 12. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

PENNSYLVANIA: *Examination*. Philadelphia and Pittsburgh, July. Act. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

TEXAS: Fort Worth, Nov. 12-14. Reciprocity applicants must be completed 30 days prior to the meeting date. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination*. Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City.

PUERTO RICO: *Reciprocity*. Santurce, Aug. 4. Sec., Mr. Luis Cueto Coll, Box 9156, Santurce.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: On application. Juneau or other towns in Territory as decided by Board. *Reciprocity*. On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

COLORADO: *Examination*. Denver, Sept. 9-10. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

DISTRICT OF COLUMBIA: *Examination*. Washington, Oct. 19-20. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

OKLAHOMA: *Examination*. Oklahoma City, August 28-29. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: Portland, Aug. 29. Final date for filing application is Aug. 12. Portland, Dec. 5. Sec., Dr. Charles D. Byrne, University of Oregon, Eugene.

TEXAS: *Examination*. Austin, October. Chief Clerk, Mrs. Sandra Allen, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination*. Madison, Sept. 19. Final date for filing application is Sept. 11. Milwaukee, Dec. 5. Final date for filing application is Nov. 27. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

* Basic Science Certificate required.

DEATHS

Hardesty, John Frank ⊕ St. Louis; born in Winfield, Mo., Dec. 31, 1887; St. Louis University School of Medicine, 1914; since 1934 associate professor of ophthalmology and since 1950 acting chairman of the department at his alma mater; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society, Southern Medical Association, and the Association for Research in Ophthalmology; formerly medical director of St. Louis Society for the Blind; fellow of the American College of Surgeons; served during World War I; on the medical advisory board of Selective Service during World War II; affiliated with St. Louis City Sanitarium, St. Mary's Group of Hospitals, Missouri Baptist Sanitarium, and Bethesda General Hospital; died June 20, aged 65, of melanoma.

Harris, Isaac Burt ⊕ Columbus, Ohio; born in Batesville, Jan. 15, 1873; Starling Medical College, Columbus, 1900; past president of the Columbus Academy of Medicine; fellow of the American College of Surgeons; joined the faculty at his alma mater, and continued on the staff when in 1914 it became Ohio State University College of Medicine, where he was assistant professor of clinical surgery from 1914 to 1925, and professor of clinical surgery from 1925 to 1946, when he retired with the title of emeritus professor; at one time a member of the city board of health; medical director and from 1915 to 1946 chief of staff at St. Francis Hospital; died in Grant Hospital, June 10, aged 80.

Hiller, Frederick ⊕ Chicago; born in Zittau, Germany, April 20, 1891; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1917; associate professor of nervous and mental diseases at Northwestern University Medical School; formerly on the faculty of the University of Chicago; specialist certified by the American Board of Psychiatry and Neurology; member of the American Association of Neuropathologists; on the courtesy staffs of St. Francis and Evanston hospitals in Evanston, Ill., and Passavant Hospital; on the staff of the Wesley Memorial Hospital; died in Evanston, Ill., June 28, aged 62, of coronary occlusion.

Wiggers, Herbert August ⊕ New York City; born in New York Sept. 26, 1907; McGill University Faculty of Medicine, Montreal, Canada, 1934; certified by the National Board of Medical Examiners; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychoanalytic Association and the American Psychiatric Association; secretary of the New York Psychoanalytic Society; treasurer of the New York Psychoanalytic Institute, where he taught at the School of Applied Psychoanalysis; consulting psychiatrist, Towns Hospital; died in Dobbs Ferry, N. Y., June 22, aged 46, of coronary disease.

Dugger, John Wesley ⊕ Jackson, Miss.; University of Tennessee College of Medicine, Memphis, 1915; past president of the Mississippi State Medical Association; member of the American Public Health Association; for many years director of the division of hygiene and factory inspection, state board of health; served as director of Pearl River County Health Unit, Marshall County Health Department, and the tricounty health district composed of Lawrence, Jefferson Davis, and Covington; died in Gulfport, June 2, aged 68, of acute coronary occlusion and myocardial infarction.

Bell, Edward, St. Louis; Meharry Medical College, Nashville, Tenn., 1916; died June 8, aged 62, of cerebral hemorrhage.

D'Amato, Charles Richard ⊕ East Rutherford, N. J.; Georgetown University School of Medicine, Washington, D. C., 1936; served during World War II; school physician; resident in radiology at the Hackensack (N. J.) Hospital; died June 5, aged 42, of coronary thrombosis.

⊕ Indicates Member of the American Medical Association.

DeMont, Charlotte, Los Angeles (licensed in California in 1917); died May 11, aged 78, of arteriosclerosis.

Dengler, Raymond Archibald, Breiningsville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1908; on the courtesy staff of Sacred Heart Hospital, where he died June 3, aged 70, of cerebral hemorrhage.

Dill, Wallace Wright ⊕ Norristown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; served on the staff of the Montgomery Hospital; died June 5, aged 76, of a heart attack.

Dunn, Joseph Francis ⊕ Chester, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1908; at one time Delaware County coroner's physician; served on the staff of the Sacred Heart Hospital; founder of the diabetic clinic at Taylor Hospital in Ridley Park; died June 11, aged 69, of pulmonary embolism.

Easom, Jack Johnson ⊕ Carthage, Miss.; Tulane University of Louisiana School of Medicine, New Orleans, 1947; died May 28, aged 33.

Edlow, Ernest S. ⊕ Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1921; died April 25, aged 56, of coronary thrombosis.

Ellsworth, Elmer Harvey, Hot Springs National Park, Ark.; Rush Medical College, Chicago, 1904; died June 2, aged 74.

Epperson, Paul Stenerson ⊕ Milwaukee; Medical College of Virginia, Richmond, 1907; specialist certified by the American Board of Radiology; member of the Radiological Society of North America; formerly assistant clinical professor of roentgenology at Marquette University School of Medicine; served during World War I; affiliated with St. Mary's Hospital; died at Genesee Lake near Oconomowoc, April 30, aged 66, of a heart attack.

Folk, John L. ⊕ Fairfax, S. C.; Medical College of the State of South Carolina, Charleston, 1888; died May 8, aged 86, of coronary thrombosis.

Fowler, Wiliam Robert, Hamilton, Texas; Arkansas Industrial University Medical Department, Little Rock, 1890; died in the Hamilton Clinic & Hospital June 9, aged 85, of coronary occlusion.

Frank, Irving Leslie ⊕ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1937; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; formerly on the faculty of Jefferson Medical College; affiliated with the Jewish Hospital and the Albert Einstein Medical Center; died June 4, aged 38.

Franklin, Abraham Lincoln, Providence, Ky.; Barnes Medical College, St. Louis, 1893; physician for the Louisville and Nashville Railroad; died May 30, aged 85.

Frisch, Frank Peter ⊕ Willmar, Minn.; University of Minnesota Medical School, Minneapolis, 1914; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; on the staffs of the Willmar Hospital and the Rice Memorial Hospital, where he died March 8, aged 68, of left ventricular failure, coronary sclerosis, cardiomegaly, and leukemia.

Gaberman, David B. ⊕ Detroit; Detroit College of Medicine and Surgery, 1920; affiliated with Florence Crittenton and Brent General hospitals; died June 12, aged 58, of heart disease.

Gellman, Isaac I., Kew Gardens Hills, L. I., N. Y.; Chicago College of Medicine and Surgery, 1914; fellow of the American College of Chest Physicians; served on the staffs of various Veterans Administration hospitals; died June 13, aged 63, of cerebral hemorrhage.

Gorr, Charles William, Chicago; Rush Medical College, Chicago, 1903; died in the Grant Hospital June 29, aged 74, of cerebral accident.

Graham, Edwin E. ⊕ Philadelphia; Jefferson Medical College of Philadelphia, 1887; emeritus professor of diseases of children at his alma mater; member of the American Pediatric Society; past president of the Philadelphia Pediatric Society; affiliated with Philadelphia General Hospital; consultant pediatrician at the Training School of Vineland, N. J.; received the honorary degree of doctor of science from Jefferson in 1950; died in Madison, Va., June 10, aged 89.

Gray, Joseph Rea Taylor Jr. ⊕ Chester, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1898; member of the American Society of Clinical Pathologists; for many years city bacteriologist; affiliated with the J. Lewis Crozer Homeopathic Hospital; died June 9, aged 83, of arteriosclerosis and myocarditis.

Green, Norman Smith, Seattle, Wash.; University of Cincinnati College of Medicine, 1943; member of the Ohio State Medical Association; formerly practiced in Cincinnati, where he was on the staffs of the Bethesda and Deaconess hospitals; died June 4, aged 40.

Hall, Harry Bolander ⊕ Boise City, Okla.; St. Louis College of Physicians and Surgeons, 1921; served as health superintendent of Cimarron County; chief of staff of the Cimarron County Hospital; died in St. Joseph Hospital, Clayton, N. Mex., May 26, aged 61, of occlusion of the basal artery of the brain.

Hall, Hugh Joseph ⊕ Providence, R. I.; Hahnemann Medical College and Hospital of Philadelphia, 1930; died in the Roger Williams General Hospital June 20, aged 56, of arteriosclerotic heart disease and diabetes mellitus.

Hanna, George Orvil, Lingle, Wyo.; Ensworth Medical College, St. Joseph, Mo., 1905; died in Scottsbluff, Neb., May 16, aged 71.

Harrison, Edwin Marriott ⊕ Chicago; Dunham Medical College, Chicago, 1902; Jenner Medical College, Chicago, 1904; Chicago College of Medicine and Surgery, 1909, and Bennett Medical College, Chicago, 1912; fellow of the American College of Surgeons; served during World War I; on the staff of the Illinois Masonic Hospital; died June 24, aged 76, of coronary thrombosis.

Hart, James Luke, Denver; University of Colorado School of Medicine, Denver, 1942; formerly affiliated with the U. S. Public Health Service Reserve; died in June, aged 35.

Hearn, Marion ⊕ Philadelphia; Jefferson Medical College of Philadelphia, 1902; died June 2, aged 78, of coronary thrombosis.

Heise, William Frederick Carl ⊕ Winona, Minn.; Rush Medical College, Chicago, 1896; fellow of the American College of Surgeons; on the staff of the Winona General Hospital; died May 29, aged 77.

Hermance, William Oakley ⊕ Philadelphia; University of Pennsylvania Department of Medicine, 1894; served on the faculty of the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; formerly clinical professor of proctology at Woman's Medical College of Pennsylvania; member and past president of the American Proctologic Society; specialist certified by the American Board of Proctology; died June 12, aged 80.

Herrick, Fred Samuel, Chicago; Bellevue Hospital Medical College, New York, 1884; died in the Illinois Masonic Hospital June 17, aged 95, of carcinoma of the prostate.

Herrington, Lewis Marion, McKees Rocks, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1901; died in Winter Haven, Fla., May 17, aged 95, of cerebral hemorrhage.

Hervey, James R. ⊕ Moorhead, Miss.; Atlanta College of Physicians and Surgeons, 1902; formerly mayor; past president of the Citizens' State Bank; died May 22.

Higbee, Frank O., Three Oaks, Mich.; the Hahnemann Medical College and Hospital, Chicago, 1894; College of Physicians and Surgeons of Chicago, 1895; served as health officer; died in Gary, Ind., June 5, aged 83, of chronic myocarditis.

Howitt, Henry Orton ⊕ San Rafael, Calif.; Cooper Medical College, San Francisco, 1887; an Associate Fellow of the American Medical Association; died in Everett, Wash., June 8, aged 90, of arteriosclerotic heart disease.

Huff, Asher DeWitt ⊕ Marion, Ind.; Indiana University School of Medicine, Indianapolis, 1932; died April 18, aged 55, of coronary occlusion.

Hussey, Cyril Christopher ⊕ Sidney, Ohio; Johns Hopkins University School of Medicine, Baltimore, 1919; affiliated with Piqua (Ohio) Memorial Hospital and the Wilson Memorial Hospital, where he died May 9, aged 59, of peritonitis and perforated duodenal ulcer.

Ingalls, Albert Thompson ⊕ Los Angeles; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; died May 1, aged 78.

Lawry, Carl C. ⊕ Earlville, Ill.; Northwestern University Medical School, Chicago, 1903; an Associate Fellow of the American Medical Association; died in Vandalia recently, aged 76, of coronary arterial disease.

Lindley, Don Carlos ⊕ New Castle, Pa.; Jefferson Medical College of Philadelphia, 1901; specialist certified by the American Board of Ophthalmology; served during World War I; on the staffs of the Jameson Memorial and New Castle hospitals; surgeon for the Baltimore and Ohio and Pennsylvania railroads; died May 8, aged 77, of coronary thrombosis.

Little, Abby Noyes ⊕ Laconia, N. H.; Woman's Medical College of Pennsylvania, Philadelphia, 1894; on the courtesy staff of Laconia Hospital, where she died May 28, aged 81, of pulmonary embolism.

Loughead, Raymond B. ⊕ Boothwyn, Pa.; Medico-Chirurgical College of Philadelphia, 1904; died May 14, aged 88.

McGrath, John Henry ⊕ Waterbury, Conn.; Yale University School of Medicine, New Haven, 1908; affiliated with St. Mary's Hospital, where he died June 15, aged 69, of coronary occlusion.

Menown, Roland R. ⊕ St. Louis; Marion-Sims-Beaumont Medical College, St. Louis, 1903; died June 10, aged 72, of coronary thrombosis.

Miles, James Oliver, Washington, D. C.; Howard University College of Medicine, Washington, 1932; during World War II volunteered his services to the Army as an examining physician of inductees and for this work was awarded a medal of recognition by the President; for many years on the staff of the Freedmen's Hospital; died June 14, aged 57.

Montgomery, Alexander ⊕ Milwaukee; Milwaukee Medical College, 1909; fellow of the International College of Surgeons and the American College of Surgeons; affiliated with Johnston Emergency and Evangelical Deaconess hospitals; died June 9, aged 66, of myocardial infarction.

Robinson, Andrew Smith ⊕ Akron, Ohio; Western Reserve University School of Medicine, Cleveland, 1914; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Industrial Medical Association; served during World War I; affiliated with City, Goodyear, and St. Thomas hospitals; died June 17, aged 63, of cancer of the lungs.

Rouse, Francis Ernest ⊕ Williamsport, Pa.; St. Louis College of Physicians and Surgeons, 1906; also a graduate in pharmacy; died May 8, aged 77.

Ryburn, John Patrick ⊕ St. Louis; National University of Arts and Sciences Medical Department, St. Louis, 1918; member of the American Academy of General Practice; on the staff of the Missouri Baptist Hospital, where he died June 8, aged 59, of coronary thrombosis.

Sansoucy, Jerome Aime ⊕ Washington, D. C.; Georgetown University School of Medicine, Washington, 1936; died June 25, aged 46, of melanocarcinomatosis.

Schuette, William Henry ✠ Mason City, Ill.; Hering Medical College, Chicago, Homeopathic, 1904; an Associate Fellow of the American Medical Association; died in Memorial Hospital, Springfield, April 10, aged 81, of injuries received when struck by an automobile.

Sheftman, Murray, Yonkers, N. Y.; University and Bellevue Hospital Medical College, New York, 1926; served during World War II; died March 16, aged 50, of acute coronary thrombosis.

Sherwood, Harry ✠ New York City; New York Homeopathic Medical College and Flower Hospital, New York, 1918; on the staff of the Mount Sinai Hospital; died March 12, aged 62.

Simpson, Carl Franklin ✠ Tulsa, Okla.; University of Louisville School of Medicine, Louisville, Ky., 1926; secretary-treasurer of the Tulsa County Medical Society for five terms; served as chief of staff of St. John's Hospital; died June 22, aged 53, of coronary occlusion.

Steinfield, Winton ✠ Yaphank, L. I., N. Y.; University of Pennsylvania School of Medicine, Philadelphia, 1941; member of the Michigan State Medical Society; specialist certified by the American Board of Internal Medicine; served during World War II; formerly on the staff of the Veterans Administration Hospital in Tucson, Ariz.; drowned in Delaware Bay off Cape May, N. J., in April, aged 35.

Swindler, Edwin Booth, Stuttgart, Ark.; Memphis (Tenn.) Hospital Medical College, 1912; died in Coral Gables, Fla., June 20, aged 70, of cerebral hemorrhage.

Thomas, Claude LeRoy, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1901; served on the staffs of Hahnemann Hospital and St. Luke's and Children's Medical Center; died June 5, aged 79, of acute cardiac dilatation.

Thompson, William Edward, Los Angeles; McGill University Faculty of Medicine, Montreal, Canada, 1882; L.R.C.P. and L.R.C.S., Edinburgh, 1886, and L.F.P.S., Glasgow, 1886; died April 4, aged 93, of congestive heart failure.

Treacy, Alfred Joseph M. ✠ Philadelphia; Temple University School of Medicine, Philadelphia, 1915; specialist certified by the American Board of Physical Medicine and Rehabilitation; served during World War I; member of the American Rheumatism Association; at one time medical officer in the contagious diseases division, city health department; died in Physicians and Surgeons Hospital June 7, aged 72, of chronic myocarditis and uremia.

Turnoff, David ✠ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1936; specialist certified by the American Board of Internal Medicine; served during World War II; associate in medicine at his alma mater; affiliated with Nazareth, Kensington, and Philadelphia General hospitals; died June 14, aged 41.

Vonnahme, Conrad Benedict ✠ East St. Louis, Ill.; Washington University School of Medicine, St. Louis, 1905; died in St. Mary's Hospital June 8, aged 72, of hemolytic anemia.

Watts, Stephen Hurt ✠ Charlottesville, Va.; Johns Hopkins University School of Medicine, Baltimore, 1901; formerly professor of surgery and gynecology at the University of Virginia Department of Medicine; member of the American Surgical Association and Southern Surgical Association; fellow of the American College of Surgeons; died in the University of Virginia Hospital June 7, aged 75, of intraventricular hemorrhage.

Webb, William Thomas, Breckenridge, Texas; Physio-Medical College of Texas, Dallas, 1906; formerly city and county health officer; died May 29, aged 79, of bronchopneumonia.

Whipper, Ionia Rollin, Washington, D. C.; Howard University College of Medicine, Washington, 1903; died April 23, aged 78.

Williams, Frederick Smith, White Plains, N. Y.; Harvard Medical School, Boston, 1903; registrar of records for the Bronx County Health Department from 1912 to 1945; died June 18, aged 78, of a heart attack.

Williamson, Cleburne Milton ✠ Corpus Christi, Texas; University of Texas School of Medicine, Galveston, 1923; died May 24, aged 59.

Willis, Morton William ✠ Jamaica, N. Y.; University and Bellevue Hospital Medical College, New York, 1932; assistant clinical professor of medicine at the New York Medical College, Flower and Fifth Avenue Hospitals; specialist certified by the American Board of Internal Medicine; affiliated with Mount Sinai Hospital in New York, Queens General, and Jamaica hospitals; died May 23, aged 45.

Wilson, George Wheeler, Captain, U. S. Navy, retired, Nevada, Mo.; St. Louis University School of Medicine, 1914; entered the Navy Aug. 4, 1920; retired April 1, 1950; on the staff of State Hospital No. 3, where he died June 9, aged 61, of coronary thrombosis.

Wolf, Charles N., York, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1889; died May 15, aged 89, of arteriosclerosis.

Wolfe, Jacob S. ✠ Bloomfield, N. J.; College of Physicians and Surgeons, Baltimore, 1890; an Associate Fellow of the American Medical Association; formerly member of the board of education and the board of health, of which he was president; affiliated with Mountainside Hospital, Montclair; died in Akron, Ohio, May 17, aged 87, of bronchopneumonia.

Woods, Robert Andrew, Pittsburgh; University of Tennessee Medical Department, Nashville, 1882; died June 22, aged 90, of complications resulting from a fall and a fractured hip.

Zwick, Karl George ✠ Cincinnati; Medical College of Ohio, Cincinnati, 1903; assistant professor of dermatology and syphilology at University of Cincinnati College of Medicine; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; affiliated with Cincinnati General and Deaconess hospitals; died May 30, aged 75.

DIED WHILE IN MILITARY SERVICE

Fidler, Albert John Eugene ✠ Commander, U. S. Navy, Coronado, Calif.; born in Allentown, Pa., April 24, 1903; St. Louis University School of Medicine, 1929; following completion of his internship at the U. S. Marine Hospital in Staten Island, N. Y., served with the U. S. Public Health Service, and from 1932 through 1942 practiced medicine in Allentown, Pa., where he was a member of the surgical staff of the Sacred Heart Hospital and of the Allentown Hospital; receiving a commission in the medical corps of the Naval Reserve in 1942, reported in May of that year to the Navy Yard Dispensary, Philadelphia, for indoctrination and duty; transferred to the regular Navy in 1946; during his naval career served aboard various ships of the Fleet and at Navy Medical Department facilities throughout the United States; in August, 1952, reported to the Naval Ordnance Test Station, Inyokern, Calif., where he was serving at the time of his death; awarded the European and Asiatic-Pacific Theater Campaign Ribbons, each with one bronze star; died June 12, aged 50, of injuries received in an automobile accident.

Wilde, Roger Conant Jr., Evanston, Ill.; born in Orleans, Vt., Aug. 27, 1927; University of California Medical School, San Francisco, 1951; after interning a year at the University of California Hospital in San Francisco was assistant resident in pediatrics at the same hospital; in October, 1952, was commissioned in the medical corps of the navy and reported for duty at the U. S. Naval Hospital in Oakland, Calif.; after a short tour at the naval base at Litchfield Park, Ariz., was sent to Pensacola, Fla., in April for flight surgeon training; lieutenant (jg) medical corps of the U. S. Naval Reserve; killed in a plane crash near Pensacola, Fla., May 26, aged 25.

GOVERNMENT SERVICES

ARMY

Following is an abstract of a statement from the Army.—ED.

Three Years of Medical Service in Korea.—During the three years of fighting in Korea, the Army Medical Service, with some help from other nations and services, had the task of maintaining the health of and caring for wounded and injured soldiers from some 15 nations of the world.

The primary interest of the Medical Service, however, was the troops of the United States Army who had come from the relatively tranquil life of occupation duty in Japan to fight a series of demoralizing battles in the extreme heat of the Korean summer, the extreme cold of the Korean winter, over frozen ridges, in insect-infested rice paddies, and through monsoons. The problem was aggravated by the hordes of refugees and homeless wanderers who jammed roads and represented a mobile source of infection and disease which was almost impossible to control.

As soon as possible after landing, the Medical Service began forceful campaigns of preventive medicine designed to halt the advance of disease and impress upon the individual soldier the need of taking necessary sanitary measures to protect himself. The result of this campaign is self-evident in the subsequent decline of the disease rates. The preventive medicine program was backed up later by regular medical inspections of troop areas, especially in the rear, to assure that proper sanitary measures were being taken.

Battle Injuries and Wounds.—The rates of occurrence for battle wounds and injuries have been far from constant during the past three years. The peak for battle casualties came in September, 1950, shortly after the offensive which carried UN forces to the Yalu River in Manchuria. At this time there were 1,187 casualties per 1,000 average strength per year. The lowest rate for casualties came in March, 1952, when 22 per 1,000 average strength per year were reported.

The fatality rate of wounded has steadily declined through the years so that now, for the three years in Korea, it has reached an all-time low of 2.3%. This figure represents a considerable drop from the 4.5% of World War II, and the World War I figure of 8.1%, excluding gas casualties.

At the same time, the proportion of wounded and injured men who have been returned to duty has increased from the World War II average of 77 for every 100 casualties admitted to medical facilities to about 88 per 100 casualties admitted. Now, however, instead of separating certain partially disabled men from the service, as was done during World War II, the Army has adopted the policy of placing these men in limited duty assignments as combat instructors, thereby minimizing manpower attrition.

Several other factors involving medical treatment have also played an important role in decreasing the fatality rate and in increasing the number of wounded and injured to be returned to duty. High on the list of factors which contribute to this lowering of mortality are the new biologicals that were available throughout the medical system from the very beginning of this operation.

The Mobile Army Surgical Hospital, an innovation since World War II, has also contributed to the lowered death rate. It brings definitive surgical treatment closer to the front lines than ever before. Recently, one of these units, designed to care for no more than 60 patients at a time, treated its 50,000th patient since the Korean conflict started.

A third factor, related directly to the specialist training program of the Army instituted in 1946, has been the complete staffing of the forward area hospitals with highly qualified surgeons and orthopedists, to an extent probably not equaled in World War II. The presence of the well-organized base in Japan, coupled with adequate air evacuation facilities that brought patients from the forward hospitals to the base hospitals in the shortest possible time, has had a definite influence. The helicopter plays an ever-increasing part in the rapid, smooth, and comfortable evacuation of seriously wounded men from the battalion aid station. The trip to a surgical hospital normally an hour or more away by ground transportation, takes only a few minutes. Helicopter ambulance units under the direct control of the division surgeon also have recently been organized.

Nonbattle Injuries.—The peak of nonbattle injuries occurred during the first winter in Korea. Cold injury—frostbite and trench foot—contributed heavily to the nonbattle casualty rates of admission during these months and was considered one of the major medical problems in Korea.

The first cold injury cases were reported in November, 1950, when the Eighth Army had forced the enemy far into North Korea near the Manchurian border where cold weather had already set in. The troops, however, were equipped with cold weather clothing and, because enemy resistance was light, the incidence of cold injury was relatively low.

When the Chinese Communists entered the war and forced the withdrawal from North Korea, however, cold injury rates soared. Troops fought and lived in temperatures as low as 25 degrees below zero Fahrenheit. Units were cut off and pinned down by enemy action. Troops suffered from exposure, loss of clothing and equipment, and lack of supply and warm meals.

Cold injury incidence reached its peak during December, 1950, when 155.4 cases per thousand average strength per year were admitted to medical facilities. Most of these cases were admitted for frostbite, but trench foot incidence was also high.

The highest monthly rate for nonbattle casualty admissions during the entire Korean campaign occurred during January, 1951, when 352 cases per thousand average strength per year were admitted. Of this number, almost half were for cold injury sustained during heavy defensive action in the Wonju-Suwan area. The remainder can be attributed to accidents involving vehicles and weapons.

To offset the high incidence of cold injury, the Army inaugurated a preventive program in Korea and cold weather indoctrination in the United States in the fall of 1950. Had this not been done, the rate would most certainly have reached more serious proportions. Indoctrination on the use of cold weather equipment was instituted as far down in echelon as company and platoon level.

Since the first winter in Korea, 1950-1951, the incidence of cold injury cases has steadily declined. The peak weekly rate during the 1951-1952 season was 51 cases per thousand average strength per year as against the peak of 293 cases per thousand average strength per year experienced during the first week of December, 1950. The most recent season, 1952-1953 appears to represent a further improvement, with the peak rate at 13.17 cases per thousand average strength per year.

Disease.—Disease has been the greatest enemy of the American soldier in Korea for the past three years, having rendered ineffective many more soldiers than have Communist bullets

and weapons. Korea is abundantly infested with insects that spread disease; lice that spread typhus and relapsing fever; fleas that carry endemic typhus; flies that carry intestinal diseases; mites that are suspected of carrying hemorrhagic fever; and mosquitoes that spread malaria. The country has an abundance of rodents that act as hosts to many of the disease-bearing insects. Refuse is generally left lying in piles or thrown into open ditches, while the disposal of waste is extremely primitive.

Korea is a nation in which disease rates reach staggering proportions. Dysentery, diarrhea, and enteritis have long caused severe morbidity. Malaria, venereal disease, and typhus fever are serious problems. Typhoid, leprosy, smallpox, and encephalitis are prevalent.

The success of the preventive medicine program of the Medical Service is attested to by simply comparing the month of August of 1950, 1951, and 1952. In August, 1950, there were 1,394 admissions per thousand average strength per year. This rate was cut by August, 1951, to 571 admissions per thousand strength and to 466 in August of 1952.

Neuropsychiatric Disorders and Treatment.—Based on late World War II experience, neuropsychiatric treatment during the Korean campaign followed three new principles: treatment as far forward as possible, centralization of screening and treatment, and the avoidance of a hospital atmosphere. By following these three principles, experience has shown that 40 to 60% of all combat neuropsychiatric casualties can be returned to duty after treatment on an excused-from-duty basis. The incidence of neuropsychiatric disorders among troops in Korea reached its peak shortly after the hostilities began in 1950 and has declined ever since.

Neuropsychiatric cases in Korea have been classed into five categories: (1) psychoneurotic disorders; (2) character and behavior disorders; (3) diseases of the nervous system; (4) psychotic disorders; and (5) all other psychiatric disorders.

Of the five classifications, that of psychoneurotic disorders has accounted for the greatest proportion of casualties, with 35.9%. Psychoneurosis is the term fitting the anxiety, dissociative, obsessive-compulsive, and depressive behavior patterns. Included in the "all other psychiatric disorders" classification, which accounts for 26.7% of all cases, are combat exhaustion and situational maladjustment. Character and behavior disorders accounted for 18.8% of the cases and is identified by alcoholism, drug addiction, and immaturity reactions. Accounting for 11.9% of all cases were cerebral hemorrhage and diseases of the nervous system such as meningitis, epilepsy and paralysis. Of all neuropsychiatric cases during the Korean campaign, only 11% have been evacuated to the United States.

Evacuation and Mobile Army Surgical Hospital.—While the saving of a great many lives can be attributed to the increased administration of whole blood, two other factors have also helped immeasurably—rapid air evacuation and the Mobile Army Surgical Hospital.

During the three years of the Korean campaign, both helicopters and large transport-ambulance planes have played an extremely important role. The little helicopter, capable of carrying two litter patients and one patient in a sitting position at a time, can go as far forward as a battalion aid station and at times even farther, pick up severely wounded soldiers and quickly fly them to a hospital near the front lines. Without them, a long and often fatal litter haul would be necessary.

The role of the larger aircraft is equally as important as the helicopter. They can take wounded men from field hospitals and in just a few hours make available to them all of the services of a large general hospital. Similarly, in just about two days these large ambulance-transports can fly wounded men from Korea to general hospitals near their homes in the United States. These planes, operated almost continually by the Military Air Transport Service, have carried thousands of men from the combat area to Japan and the United States.

The small Mobile Army Surgical Hospital, a post-World War II development, offers severely wounded men definitive surgery shortly after they have been hurt, often within a few minutes. Located in a division area near the front line, the hospital receives patients by helicopter and ambulance, provides them with immediate surgery, and keeps them until they can safely be evacuated further to the rear.

Originally designed to care for 60 patients at a time, many of these little field hospitals have taken care of hundreds of patients at a time. A typical unit is composed of 14 physicians, 12 nurses, 2 Medical Service Corps officers and 97 enlisted men.

It usually sets up in the field in much the same manner as a circus. In addition to its tentage, the hospital unit carries with it sufficient organic transportation so that it can move itself from place to place without help from another source. This versatile hospital can be dismantled and all of its equipment can be packed and moved from a location in less than three hours. Thirty minutes after arrival at the new location, a patient can be on an operating table undergoing major surgery and the entire hospital can be functioning less than four hours after arrival.

Personal.—Brig. Gen. Sam F. Seeley will soon leave his position as chief of surgery at the Walter Reed Army Medical Center in Washington, D. C., for a new assignment with the Office of the Chief Surgeon, U. S. Army, in Europe headquarters. A graduate of the University of Nebraska and the University of Minnesota Medical School, the general entered the Army in 1927.

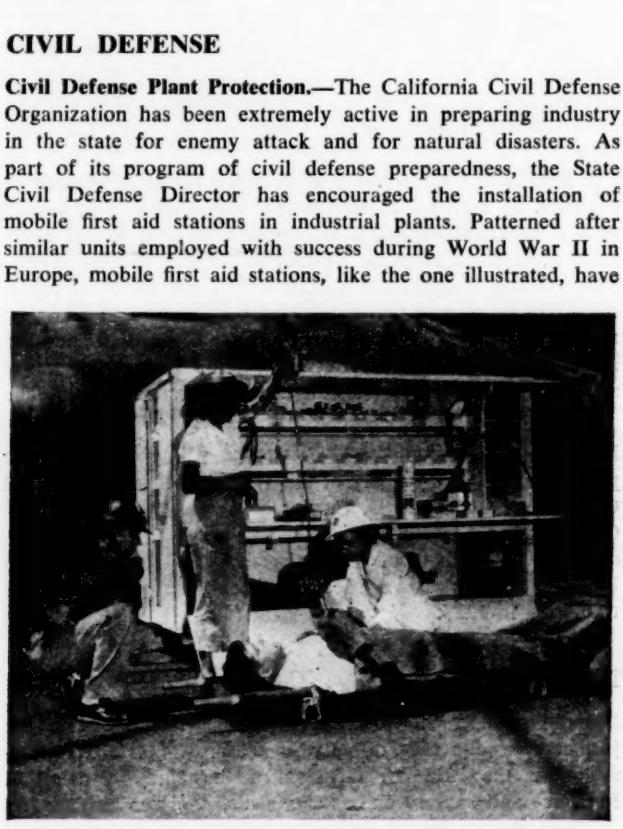
NAVY

Personal.—Capt. C. W. Shilling (MC), U. S. N., who has just completed a tour of duty in Washington, D. C., as director of the Research Division of the Navy's Bureau of Medicine and Surgery and as special assistant for Bio Sciences in the Office of Naval Research, is now the senior medical officer at the U. S. Naval Academy, Annapolis, Md. Dr. Shilling was recently awarded the Founder's Medal of the Association of Military Surgeons of the United States for his outstanding contribution to military medicine.——Capt. O. D. Yarbough (MC), U. S. N., a qualified submarine officer, became the director of the Research Division of the Bureau of Medicine and Surgery. Prior to reporting to his present assignment he was force medical officer of the Staff of the Commander, Submarine Force, U. S. Pacific Fleet.——Capt. C. P. Phoebus (MC), U. S. N., reported as special assistant for Bio Sciences at the Office of Naval Research. A qualified naval aviator, prior to coming to his present assignment, Dr. Phoebus was head of the Medical Military Specialties Branch and Aviation Medicine Section of the Research Division of the Bureau of Medicine and Surgery——Capt. Leon D. Carson (MC), U. S. N., the director of the Aviation Medical Acceleration Laboratory at the Naval Air Development Center, Johnsville, Pa., has been appointed a visiting professor of aviation physiology, in the School of Medicine, University of Pennsylvania. He was reappointed as a lecturer in the Graduate School of Medicine in aviation physiology. At the same meeting of the Trustees, Capt. Charles F. Gell (MC), U. S. N., the deputy director of the Aviation Medical Acceleration Laboratory at the Naval Air Development Center, Johnsville, Pa., was reappointed as assistant professor in physiology in the School of Medicine and lecturer in the Graduate School of Medicine. ——Dr. Howard T. Karsner, medical research adviser to the Surgeon General of the Navy, has been appointed chairman of the Advisory Medical Board of the Leonard Wood Memorial

(the American Leprosy Foundation). In addition to this appointment Dr. Karsner was recently appointed as a member of the Committee on Medical Research of the American Trudeau Society, which is the medical section of the National Tuberculosis Association. Also, he was reappointed as chairman of the Committee on Pathology of the Division of Medical Sciences, National Research Council.

CIVIL DEFENSE

Civil Defense Plant Protection.—The California Civil Defense Organization has been extremely active in preparing industry in the state for enemy attack and for natural disasters. As part of its program of civil defense preparedness, the State Civil Defense Director has encouraged the installation of mobile first aid stations in industrial plants. Patterned after similar units employed with success during World War II in Europe, mobile first aid stations, like the one illustrated, have



Mobile first aid station for protection of industrial plants.

been built and installed throughout the facilities of the San Diego Consolidated Vultee Aircraft Corporation. The units are kept supplied and ready at all times for possible emergencies. They are also used during civil defense drills, as illustrated.

PUBLIC HEALTH SERVICE

Water Pollution.—According to the Public Health Service, the nation's municipalities invested about 31 million dollars in water pollution control projects during the first quarter of 1953. Contracts were awarded for 119 sewage treatment projects designed to keep harmful wastes out of rivers, lakes, and other waterways. Of these, 61 are for construction of new sewage treatment plants, 48 for enlargement or improvement of existing plants, and 10 for construction of interceptor sewers.

Local Health Services.—As of July 1, 1952, there were 1,333 health organizations providing full-time local health services in the United States, according to the Public Health Service. These organizations service 1,637 counties, include 279 cities, and cover areas with a combined population of about 120 million. These figures represent an increase over the previous year of 40 organizations, 95 counties, 3 cities, and about 7 million persons with full-time local health services.

Personal.—Dr. Clifton K. Himmelsbach has been appointed assistant chief, Division of Hospitals, Public Health Service, Department of Health, Education, and Welfare. Formerly medical officer in charge of the U. S. Public Health Service Outpatient Clinic in Washington, D. C., Dr. Himmelsbach succeeds Dr. Myron D. Miller, recently assigned as medical officer in charge of the U. S. Public Health Service Hospital, Seattle. As assistant chief of the Division of Hospitals, Dr. Himmelsbach's new responsibilities involve the administration of the 16 hospitals and 125 outpatient facilities that comprise the medical care program for legal beneficiaries of the Public Health Service.

VETERANS ADMINISTRATION

Reorganization.—The reorganization of the Veterans Administration will become effective Sept. 7, 1953, according to acting administrator H. V. Stirling. The three operating officials designated were Adm. Joel T. Boone to continue as chief medical director responsible for the Department of Medicine and Surgery including special services, which was previously a separate operation; Charles G. Beck who will become acting deputy administrator for insurance with responsibility for the reorganized Department of Insurance; and E. E. Odom, now chief legal officer of the Veterans Administration with the title of solictor, who will be the acting deputy administrator for veterans' benefits. As head of the new department the latter will be responsible for all benefit programs including compensation and pension, vocational rehabilitation and education, loan guaranty, guardianship, and contact. Frank W. Kelsey, presently assistant administrator for finance, will be acting controller in the new organization. The budget, audit, accounting, reports and statistics, and policy and planning services will be under his direction. Frank R. Kerr, now assistant administrator for personnel, was designated to fill the new position of acting assistant administrator for administration. He will be in charge of the personnel, purchasing, administrative, and security services. Frank H. Dryden, presently assistant administrator for construction, supply and real estate, will be acting assistant administrator for construction. The only position for which no acting official was designated is the office of general counsel.

Personal.—Managers for the new 1,000-bed neuropsychiatric VA Hospital nearing completion in Salisbury, N. C., and for the existing 200-bed general medical and surgical VA Hospital in Saginaw, Mich., have been appointed. The new hospital in Salisbury will be managed by Dr. Louis F. Verdel, who, since 1944, has been manager of the VA Hospital in Northport, Long Island, N. Y. Dr. Edward H. Mandell, who since April, 1951, has been assistant chief of professional services at the VA Hospital in Minneapolis, becomes manager of the VA Hospital in Saginaw. In addition he will serve as chief of professional services. He succeeds Dr. Morley B. Beckett, recently transferred to the new VA Hospital in Ann Arbor, Mich.

MISCELLANEOUS

Personal.—Dr. Alan T. Waterman, director of the National Science Foundation, has announced the resignation of William A. W. Krebs Jr. as general counsel of the foundation and the appointment of William Jay Hoff, former assistant to the director of the Office of Defense Mobilization and assistant administrator of the Defense Production Administration, to the vacancy.

FOREIGN LETTERS

BRAZIL

Anesthesia in Intrathoracic Surgery.—Dr. Fernando Paulino, head surgeon of the Casa de Saúde São Miguel, published in *Revista Brasileira de Cirurgia* (24:699 [Nov.] 1952) a report on the anesthesia used in 185 consecutive intrathoracic major operations, excluding thoracoplasties and pleurotomies. This is the largest series ever reported in Rio de Janeiro in this field of surgery and does not represent specially selected operations but the total of operations of this kind performed by a specialized surgeon since the founding of that hospital. The total of 185 operations includes 56 cases of pneumonectomy and lobectomy, 32 of esophagectomy and gastrectomy, 40 of thoracolumbar sympathectomy, 25 of exploratory thoracotomy, 3 of mitral valvulotomy, 12 of operations on the esophagus for such conditions as diverticula, atresia, and anastomosis, and 17 others including surgery for mediastinal tumors, diaphragmatic hernioplasty, and pulmonary decortication.

The author discusses the problem of surgical fatality and establishes a distinction between deaths during surgery and those that occur later. A first fact is important: out of the total of 185 patients anesthetized for intrathoracic operations, none died in the operating room. All patients left the operating room in satisfactory general condition and were safely transported to bed. The author points out that the group included patients of less than a month old, a few only two to three days old, and others older than 75; some of the latter had arterial hypertension, cardiovascular lesions, and advanced neoplasms. Dr. Paulino believes that, in the field of intrathoracic surgery, it is an acceptable criterion to include as immediate surgical deaths all those that occur within 10 days after the operation. In this situation, he had eight deaths (4.3%), occurring from four hours to five days after the operation, in cases of atresia of the esophagus, cancer of the esophagus, pulmonary cancer, pulmonary abscess, and hypertension.

In the author's cases all the well-established principles of the technique of anesthesia with tracheal intubation and manually and mechanically controlled respiration were followed. Thiopental (Thionembutal) sodium, nitrous oxide, or nitrous oxide-curare were used for the induction of anesthesia and variable mixtures of ether, oxygen, curare, nitrous oxide, and meperidine (Demerol) hydrochloride for its maintenance. The anesthesia was administered with McKesson's and Heidbrink's apparatus, or with the Espiropulsator and the Pulmoflator. According to the author, the good clinical results cannot be attributed to individual anesthetics or to particular equipment, since these factors varied in different cases, with similar results. He is sure that the three main reasons for the success were (1) the great experience of the anesthetist; (2) the exact blood replacement during the operation; (3) the rigid observance of the physiological principles well established for the compensation of the rupture of the respiratory equilibrium caused by thoracotomy (controlled respiration, tracheobronchial suction, adequate oxygenation and ventilation, and blocking of inconvenient reflexes).

Clinicopathological Study of Pheochromocytoma.—Drs. José Schermann and M. Barretto Netto, of the department of endocrinology, Rio de Janeiro University, reported what seems to be, in the medical literature of Brazil, the first case of pheochromocytoma clinically diagnosed in which surgery was successfully employed and hormonal assays of the tumor obtained. The patient had a typical adrenosympathogenic syndrome with crises appearing under the effect of different kinds of stimulation such as emotions, exertion, prolonged fasting, and abdominal palpation. As complementary symptoms suggesting a chromaffin tissue tumor there were hyperthermia, increase of basal metabolism, and abnormal glycose tolerance, which disappeared after the operation. The histamine test was negative, and the tetraethylammonium chloride test caused a characteristic rise in blood pressure. Particularly helpful for the diagnosis was the perirenal x-ray picture after oxygen insufflation through the presacral space, associated to descendant pyelography, which disclosed a right suprarenal tumor causing a downward displacement of the kidney.

Surgery, with the patient under cyclopropane-curare anesthesia with tracheal intubation, permitted good access through the transpleural route and easy extraction of the tumor. A paroxysmal hypertensive attack occurred during the opening of the pleural cul-de-sac but disappeared spontaneously within a short time. Twice during the postoperative period, a low blood pressure crisis was successfully treated by intramuscular injections of Coramine (a 25% solution of nikethamide) ephedrine, blood transfusions, hydration, Adreno-cortin (an adrenal cortex extract), and strophanthin. The extirpated tumor, weighing 90 gm. and presenting a typical macroscopic aspect, showed at the histological examination characteristic alterations with staining reactions peculiar to the chromaffin tissue. The hormonal analysis of the pheochromocytoma, using von Euler and Hellner's chromatographic method, demonstrated the presence of 2.3 mg. of arterenol per gram of tissue, totaling 207 mg. for the whole tumor. The pharmacodynamic study of the patient's urine showed the presence of 1 mcg. of the hormone per milliliter. Three months after the operation the patient was found in perfect physical condition.

Fatal Hemorrhagic Syndrome in Thoracic Surgery.—Drs. E. Rocha Jr., Isaac Malogolovkin, and E. Marques Tinoco discussed recently two fatal cases of hemorrhagic syndrome, which occurred in a series of 42 intrathoracic operations performed at the Rio de Janeiro Policlinica Geral, representing an incidence of 4.76%. The two fatal accidents are attributed by the authors to a hemorrhagic fibrinolytic afibrinogenemic syndrome. By a careful analysis of the results of the preoperative examinations as well as all the information concerning the operations the authors are sure they can rule out the influence of blood transfusions as well as the possibility of transfusion accidents. Similarly, the absence of coagulability could not be related to an excess of heparin, as it can be deducted from the lack of result of the treatment with protamine sulfate and from the negative result of a later in vitro test. The authors believe that the most probable diagnosis of the cause is massive hemorrhage by afibrinogenemia. They suggest the interference of the liberation, through the lungs, of a fibrinolytic enzyme, acting as a precipitating factor, in consequence of the surgical manipulation.

ITALY

Surgical Transplants.—At the meeting of the Ionic Society of Medicine and Surgery on Dec. 14, 1952, Prof. Paolo Buonsani, the president of the society, read a paper on surgical transplants. It is impossible to replace tissue in man with tissue that is biologically more active or differs greatly histologically. There is a defense reaction by the host tissue against the graft, even against tissues that do not differ greatly although they are more likely to "take." This immunogenic or allergic reaction dooms the graft to eventual replacement by the host's tissues. The incompatibility is less pronounced in autoplastic than in heteroplastic grafts.

The ease with which an avascular transplant takes, as in the cornea and the cartilages, indicates the relative unimportance of the blood supply. In fact, when entire visceral organs are grafted by anastomosis, severe toxicosis of the host results from absorption of the products of decomposition.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Considering that the histopathological process of the graft consists of an inflammatory process similar to the healing of a wound, it can be inferred that the host must first eliminate the necrotic tissue through leukocytic action and then restore the "guide-system" through the lymphocytes. The graft does not regain its neurotrophic capacity.

The former belief that gonadal grafts continue to function must be attributed to the fact that transplanted glands of internal secretion produce a transitory functional or therapeutic effect as a result of catabolic processes, but eventually they become exhausted.

Therefore, it can be said that, although tissues not markedly differentiated from the host tissue give excellent clinical results in grafting procedures, transplantation of vital organs appears difficult. In fact, in the case of arterial transplants they cannot be said to be successful. On the other hand, according to Seddon, the recuperative power of nervous tissue is astonishing.

Sciatica Due to Disk Lesions.—On March 20 Prof. Paride Stefanini, director of the University of Perugia surgical clinic, read a paper at the Rome Medical Academy on the sciatica originating from lesions of the intervertebral disks. Prof. Cesare Frugoni was chairman of the meeting. Professor Stefanini recalled that it was at the Rome Medical Academy in 1941 that he reported on the first two patients with sciatica who recovered after an operation for herniation of the disk. He emphasized that sciatica should not be considered as neuralgia or the pain of neuritis but as the clinical equivalent of a root pain. Its cause may be compression, edema, infiltration, or inflammation, but it can always be demonstrated in essential sciatica. Clinically the radicular origin is demonstrated by the typical root distribution of the spontaneous pain and the paresthesias and disturbances of sensitivity that careful examination almost always reveals in patients with lumbar sciatica. When present, the motor disturbances, which are not too frequent, have a radicular distribution also, while the electrodiagnostic examination reveals a radicular lesion.

Professor Stefanini called attention to the three characteristics of sciatica. 1. It is a disease of one or two roots that usually involves the fifth lumbar and the first sacral roots. 2. The clinical picture does not vary. 3. The patient with sciatica has or has had backaches; sciatica is related to lumbago, just as the sciatic nerve has its origin in the lumbosacral roots. This accounts for the rigidity and the classic defensive position of the trunk in persons with sciatica.

Since the clinical picture is so well defined, it seems probable that the lesion in the lumbosacral roots is constant and characteristic. The question naturally arises of whether sciatica is always due to hernia of the disk. Many authors believe it is; others think that it should be attributed to hernia of the disk only in a certain percentage of cases; others deny this principle and believe that hernia of the disk is a defense of the vertebral column in patients with sciatica. This disagreement of opinions results from the fact that herniation of the disk was not found in every case of sciatica at operation. Professor Stefanini pointed out that degeneration of the nucleus pulposus, cartilages, and annulus occurs in intervertebral disks, especially in the lower part of the vertebral column. Alterations of the intervertebral ligaments may occur in addition to herniation.

Sciatica occurs only when the degeneration is so pronounced that the nucleus pulposus herniates. To support this concept, Professor Stefanini discussed factors that cause him to attribute backache and sciatica to degeneration and hernia respectively. Vertebral pain can also originate in the disk lesion, as can acute sciatica, which can be attributed to sudden protrusions of the disk. Objections to this concept are based on the fact that a trauma is not present in all cases. If previous degeneration is assumed, however, one of the usual and small traumas of every day life would be sufficient to cause protrusion. There is a history of trauma in 50% of the patients with disk hernias, and it is always present in sciatica of sudden onset.

Professor Stefanini refuted the objections based on the negative surgical findings and emphasized the technical difficulties. As for the objection that many patients with sciatica recover with medical treatment, he said that many patients who consider themselves cured or only slightly ill are susceptible to sudden aggravations. On the other hand, even patients who have a definite hernia of the disk often improve spontaneously. These sudden improvements are understandable if it is considered that the pain results not only from compression but also from the effects of other factors (such as infection) that act on the distended root. The role of these other factors may explain why hernia of the disk may be present without pain and that many conditions, such as cold, poisonings, and infections, may erroneously appear to be the cause of sciatica.

Finally Professor Stefanini discussed the principles of selection of treatment for sciatica. Operation should not be performed immediately; in fact, most patients are benefited by medical therapy, bed rest, and physical therapy. When such treatment is not sufficient, a plaster or orthopedic back brace is advisable. In persistent cases surgical treatment should be undertaken. Professor Stefanini reports good or excellent results in about 80% of approximately 200 operations he has performed.

Society of Cardiology.—At a meeting of the Italian Society of Cardiology on March 25, Dr. Boldrini spoke on urinary excretion of riboflavin and the influence of cocarboxylase on the urinary excretion of riboflavin in cardiac decompensation. He had previously observed that administration of digitalis increases the excretion of riboflavin abruptly, while the lactacidemia and pyruremia values rise in an inverse ratio to the riboflavinuria. Since digitalis restricts urinary excretion of thiamine in congestive decompensation, Dr. Boldrini thought that probably in the presence of digitalis the phosphorus radicals with a high energy-producing power are preferably used for the phosphorylation of the thiamine. In other words, he thought that in cardiac decompensation there is also a disturbance in phosphorylation. This hypothesis is supported by the sensitivity of the high blood levels of pyruvic acid found in cardiac decompensation to cocarboxylase and not to thiamine.

To verify the influence of cocarboxylase on urinary excretion of riboflavin, he administered 100 mg. of diphosphothiamine intravenously to six patients with heart disease who were receiving digitalis. The urinary riboflavin values decreased immediately to 70% of the initial values and increased again slowly during the following days. Since this decrease has also been observed in patients with other conditions (such as infectious disease) who were receiving cocarboxylase, Dr. Boldrini believes they also had disturbances of phosphorylation that interfered with the metabolism. Thus, riboflavin that was not utilized was eliminated through the kidneys.

Focal Oropharyngeal Infection and Renal Function.—At a meeting of the Medical and Surgical Society of Pisa, Nov. 21, 1952, Drs. Fiaschi, Grassi, and Andres reported results of their studies of the effect of focal oropharyngeal infection on renal function. They used the sodium thiosulfate clearance rate to determine the rate of glomerular filtration; the sodium para-amino hippurate clearance to measure the renal blood flow and the maximal tubular excreting capacity; and the urea clearance and the endogenous creatinine clearance to measure the tubular reabsorption of water.

The studies were made on 12 patients with oropharyngeal, dental, and tonsillar infection, 7 of whom did not have impairment of the kidney function according to results of an Addis count. The other five patients had signs of acute or chronic glomerulonephritis.

In the seven patients with normal kidney function results of tests for kidney function remained normal after any procedure such as surgical drainage. In the patients with glomerulonephritis, however, any procedure involving the focus of infection was followed by a sudden decrease of glomerular filtration. The changes in the tubular function were much less noticeable. These sudden and pronounced modifications of the glomerular function and kidney circulation were not prevented or even modified by administration of drugs that have a ganglioplegic or sympathicolytic action.

International Symposium on Vitamins.—One of the important recent conventions was held at the Milan Technical Museum where all the astonishing mechanical and technical drawings of Leonardo da Vinci are housed. Luigi Einaudi, president of the Italian Republic, read the inaugural address. Among the foreign representatives were Henrik Dam, Nobel prize winner from the Polytechnic Institute of Copenhagen, W. H. Scopfer, director, University of Bern (Switzerland) Institute of Botany, Georges Mouriquand, director, University of Lyon (France) Pediatric Clinic, and Alfred Vannotti, director, University of Lausanne (Switzerland) Medical Clinic.

Prof. Sabato Vasco, director, National Institute of Nutrition, who was introduced by Professor Colonnetti, president of the National Council of Research, read a paper on the evolution of the concept of vitamins. He said that the vitamins have great biochemical importance and that the action of digestive enzymes depends on the presence of vitamins.

Dr. Aykrod reviewed the history of the discovery of vitamins. Professor Usuelli, director, University of Milan Institute of Zootechny, reported on use of vitamins in animal breeding. Professor Amantea, director, University of Rome Institute of Physiology, reported on the requirements for vitamins in the body.

On the second day, Prof. F. Cedrangolo, director, University of Naples Institute of Medical Chemistry, discussed the biosynthesis of nicotinic acid in animal tissues. He reported on numerous experiments carried out in his laboratory that show that neither tryptophan nor its various metabolites can produce nicotinic acid or pyridine in living tissues or in eggs during incubation. It appears doubtful to him that animal tissues are able to convert tryptophan into nicotinic acid without any bacterial participation.

Prof. P. Di Mattei, director, University of Rome Institute of Pharmacology, discussed the antagonism between drugs that cause avitaminosis and vitamins and the action of vitamins when particular drugs are administered.

Professor Vannotti, Lausanne, Switzerland, reported on vitamins and enzymes from the clinical point of view. The biological action of the vitamins is intimately related to their enzymatic function. Certain vitamins (B complex) differ from the others in that, when they are partially transformed in the organism (by phosphorylation) and joined to a protein, they form cellular ferments and participate as co-enzymes in the regulation of metabolism of carbohydrates, proteins, and fats. Disturbances of the function of these ferments are due to either a deficiency or too great a utilization of the corresponding vitamins or to their insufficient transformation into ferments.

Professor Schopfer, from the University of Bern, reported on antivitamins, which are specific competitive antagonists of the vitamins. Their effect consists in displacing the vitamins, thus hindering the activity of the enzymes of which the vitamins are the co-enzymes. The resultant interference with metabolic processes has repercussions greater than simple displacement: disturbances in the biosynthesis of certain acids, purines, nucleic acids, and other essential metabolic products are increased. In certain micro-organisms it can be shown that not only the specific vitamin corresponding to the utilized antivitamin is displaced but the whole vitamin balance of the organism is disturbed. The avitaminosis caused by an antivitamin is, therefore, apparently similar to that which is secondary to irradiation. While antivitamin avitaminosis does not damage the physiological genotype, avitaminosis due to irradiation does damage the genome.

The point of view presented by Schopfer has great importance. Schopfer compared the effect of antivitamins to avitaminosis due to "mutation" of the enzyme resulting from irradiation that results in cellular inability to synthesize vitamins being transmitted from generation to generation. There is no doubt that this concept will affect the interpretation of some phenomena of enzymatic "deviation" that are typical in cancer. It is known that the enzymatic alterations in cancer are always the same no matter what organ is affected, whereas each healthy organ has its own, different enzymatic system.

Prof. G. Frontali, University of Rome, read a paper on vitamin overdosage. He reported on severe cases of overdosage of vitamin D_2 (300 cases have been reported in the world literature and 17 were fatal), vitamin A (20 cases in the world literature), and vitamin B complex (pronounced toxic manifestations). He proposed that concentrated vitamin preparations be labeled with safe maximal doses and safe intervals between doses. Greater than usual doses should be supplied only on medical prescription.

Henrik Dam, Nobel prize winner, discussed vitamins and antivitamins in blood coagulation. Since 1936 the formation of prothrombin in the body has been known to depend on the supply of vitamin K, and since 1941 to be inhibited by bishydroxycoumarin (Dicumarol). Since 1943 a series of new coagulation factors has been discovered, making modification of the theory of blood coagulation necessary.

Vitamin K and bishydroxycoumarin were originally believed to be simple antagonists. The following observations, however, were incompatible with such a view: Under suitable conditions mixtures of bishydroxycoumarin plasma and plasma deficient in vitamin K coagulate faster than either of the two plasmas alone. In addition, methylnaphthoquinone is almost unable to compensate for the anticoagulation effect of bishydroxycoumarin. The latest theories of blood coagulation and the recent observation that vitamin K_1 compensates efficiently for the action of bishydroxycoumarin have given more ground for the theory of competitive antagonism. Recently it was shown that vitamin K_1 acts much faster than methylnaphthoquinone in simple vitamin K deficiency, and this observation is probably related to the superiority of vitamin K_1 in counteracting the anticoagulant effect of bishydroxycoumarin.

Other papers were read by Professors Chini, from the University of Bari, and Sotgiu, from the University of Rome. Four hundred persons participated in the convention. Among the Americans present was Dr. Clive M. McCay (State College of Agriculture, Cornell University, Ithaca, N. Y.), who read a paper on the evolution of vitamin needs from insects to man.

LONDON

The Queen at the Royal College of Surgeons.—On May 8 the Queen attended a ceremony at the Royal College of Surgeons in London at which she laid a stone containing a casket in which was a Calender of the College and other documents. The president of the college, Sir Cecil Wakeley, welcomed the Queen, and the Bishop of London dedicated the memorial stone. Work on the College of Surgical Sciences (endowed by Lord Nuffield) is to start shortly. The new Great Hall will seat 700 persons and provide a center for surgical congresses, lectures, or social occasions. Above it will be three floors of museums, and departments of anesthesia and dentistry will be provided.

Prescribing Under the National Health Service.—During the first year of the National Health Service, family physicians' prescriptions cost 35 million pounds. This year it is estimated that the cost to the taxpayer will be some 10 million pounds more. Nevertheless, in the summarized accounts of the National Health Services the Auditor-General states that only 282 family physicians were reported for apparent excessive prescribing. All but 11 reduced their prescriptions after a warning "without detriment to the treatment of patients." Now the *British Medical Journal* (**1**:1040 [May 9] 1953) points out that no departure must be made from recognition of the fact that the physician is the sole arbiter of what is best for his patient.

The Medical Defendant.—A leading article in the *Lancet* (**1**:887 [May 2] 1953) under this heading draws attention to the fact that medical practitioners are apparently being made the target in increasing numbers of claims based on allegations of negligence. Among the reasons put forward is that it may be an inevitable feature of a health service in which

members of hospital staffs are known to be paid. Of course, there is another national service—the free legal aid scheme —in which the plaintiff has access to absolutely free legal aid and advice and loses nothing. Whatever the reason, *Lancet* points out quite correctly that the practitioner, as the menace of writs for damages grows, may be inclined to play for safety when a bold course might help the patient more. The old adage "better a living problem than a dead certainty" may yet become reversed.

Immunization in Diphtheria Outbreak.—In the *British Medical Journal* (1:964 [May 2] 1953) Drs. Lycett and George describe an outbreak of diphtheria that occurred in Staffordshire in 1951. Of 108 patients, 6 died. It was found that the outbreak coincided with a low level of immunity among the child population and the incidence fell after mass immunization, which was accepted willingly by the public confronted with an outbreak of diphtheria. In the 22 severe cases of diphtheria, only 7 patients had been immunized, although none had received a reinforcement dose, and of the patients who died none had been immunized.

The New Year Honors.—The list of medical men awarded honors in the New Year Honour List includes names known all over the world and also names known only in Great Britain. All have deserved this honor, and the public recognition is gratifying to the profession to which they belong. An outstanding man of science and surgeon, Prof. Wilder Penfield enters the Order of Merit, limited in numbers to 24, the two other medical members being Dr. E. D. Adrian and Sir Henry Dale. Professor Penfield was born in America and subsequently became a naturalized Canadian citizen. Before and after the 1914-1918 war he was a Rhodes Scholar at Oxford, where he studied under Sir Charles Sherrington. The titles of his principal publications, "Cytology and Cellular Pathology of the Nervous System," "Epilepsy and Cerebral Localization" (with T. C. Erickson), and "The Cerebral Cortex of Man," show the nature of his contributions to medical science and neurosurgery.

Mount Everest Expedition.—A radical change in the footwear of this year's British Mount Everest expedition is announced. Instead of the familiar heavily nailed, leather climbing boots, the assault parties will wear a much lighter boot with soles of artificial rubber and glacé kid uppers. The boots are insulated inside with a layer of kapok nearly an inch thick. It is pointed out that lightness and warmth are far more important qualities than durability and water-resistance for the Everest assault. The boots, which have already been tried in the Alps, will be required only for a few days' use, and at the temperatures high on Everest water is unlikely to be encountered.

Patients' Charter Seeks Later Hospital Waking.—Later waking is one of many recommendations made in a charter for hospital patients published recently. It is contained in a report to Mr. Macleod, Minister of Health, by the Central Health Services Council. This is a standing body that advises the minister on the National Health Service. Under a lay chairman, Mr. F. Messer, Socialist M.P. for Tottenham, it is composed of representatives of every branch of medicine. "One of the strongest complaints from patients," the report says, "is that the waking hour, apparently without reason, is too early in the morning."

To remedy this, some tasks traditionally performed before physicians' rounds should be done during or after them. "No patients apart from those receiving special treatment should have to be awakened before 6 a. m. and later if possible." Meals should be punctual and suitably spaced. It was not unknown for patients to have nothing between 6:30 p. m. and 8:30 next morning. The unwritten rule that meals should not be served while a physician is visiting a patient should be abolished. There should be a wide choice of food, with both small helpings and second helpings available. A teapot for each patient, with separate milk and sugar, should be the aim.

Hospitals should remember that patients have personalities of their own, and are not merely cases. Since the creation of the National Health Service they have been less willing to accept instructions without question and more responsive to sensible explanations and requests for help. "Medical and nursing staff and administrators should not maintain the attitude of 'theirs not to reason why' which was occasionally adopted towards those dependent on charity or the rates." Voluntary work has a permanent and important place in National Health Service hospitals. "We are glad to see how widely this is recognized."

British Medical Association.—The British Medical Association has this year raised its annual subscription to six guineas ($17.64). In view of what is regarded as the usual effect of such an action on the membership of the association, it is interesting to note the effect. Every year there is a certain number of resignations, which usually fluctuates between 300 and 500; this year it is just over 1,000. But since Jan. 1, 1953, 480 new members have joined, compared with 270 in the same period the previous year.

Physicians Divided Over Practices.—The General Medical Services Committee, which negotiates on fees and conditions for the 20,000 family physicians in the National Health Service, has decided against asking for restoration of the right to buy and sell the good will of practices. Many physicians, notably the 3,000 in the Fellowship for Freedom in Medicine, of which Lord Horder is chairman, believe restoration is essential if defects in the service are to be remedied. Some would make it optional. The committee regards the proposal as impracticable. It will declare itself as not in favor of action along these lines. There is strong feeling on both sides on this issue.

Psittacosis in Britain.—It has long been known that human beings are susceptible to an infectious disease of parrots called psittacosis. The disease is caused by infection with a virus, and in addition to birds of the psittacine group in which parrots, cockatoos, and budgereegahs are included canaries, pigeons, domestic fowls, and ducks all harbor these organisms and have been responsible for infection in man. In 1930, after a serious outbreak of psittacosis, with many deaths, a complete ban was imposed on the importing of parrots into this country. The ban was raised in December, 1951, and it is likely that a number of infected parrots have since been introduced. Indeed, the death on Dec. 4, 1952, of the manager of a pets' corner in a department store was shown at the inquest at Birmingham to be caused by psittacosis acquired from infected parrots in a consignment of birds that he had received in November.

TURKEY

Ascarides Perforated Intestines.—In volume 10 of *Bursa Klinik* Dr. Feridun Timur, chief of the Kutahya General Hospital medical department, reports a case of perforation of the intestines caused by ascarides with resultant peritonitis. The patient, a 30-year-old farmer, had suffered acidity of the stomach, profuse salivation at night, and itching of the nose for five years. Twelve days prior to admission to the hospital the patient felt an abdominal pain that gradually increased; constipation, nausea, and vomiting began, and the pain in the abdomen became unbearable. On admission to the hospital the patient was in a coma and had a temperature of 38.5 C, a pulse rate of 130, hallow cheeks, and a greatly distended abdomen. The blood cell count revealed 3,400,000 red blood cells and 6,000 white blood cells. The differential count revealed 70% polymorphonuclear cells, 21% lymphocytes, 5% transitionals, and 4% monocytes; the sedimentation rate was 32 mm. after one hour; and urinalysis did not reveal anything abnormal. Laparotomy under thiopental (Pentothal) sodium anesthesia was performed by hospital chief surgeon Dr. Osman Dirim. The abdominal cavity revealed seropurulent liquid and at the end of the ileum, about 50 cm. above the ileocecal

valve, a 5 mm. perforation. Other than intestinal hyperemia there were no pathogenic conditions of the intestines. One Ascarid micro-organism was about to pass through the perforation into the peritoneum where several more ascarides were found. Palpation revealed the presence of ascardes in the intestines, but the intestinal passage was free. The abdominal cavity liquid did not reveal ascarides eggs. The intestinal perforation was closed with nonaborbable surgical suture, and a large tube was inserted into the abdomen. Recovery, after 25 days, was uneventful.

Tuberculosis Among Primary School Children.—In *Bursa Klinik,* volume 10, Dr. Neshati Üster, chief of the tuberculosis hospital, his associate Dr. Reha Zeybeker, and Dr. Celil Uygun have published the results of their five year investigation concerning BCG prophylaxis and tuberculosis among primary school children of Bursa City. Twenty-eight schools with 8,800 children were investigated. Tuberculin tests resulted in 21.6% to 61.4% positive reactions. The first grade, 6-year-old children had positive Pirquet reactions in 21.6% of the cases, the 7-year-olds 27.2%, the 8-year-olds 31.4%, the 9-year-olds 37.1%, the 10-year-olds 41.5%, the 11-year-olds 43.2%, the 12-year-olds 49.8%, the 13-year-olds 55.3%, the 14-year-olds 61.4%, and the 15-year-olds 60%. Of 5,139 boys 39.5% had positive Pirquet reactions, and of 3,661 girls 37.5% had positive reactions. According to the grades, positive reactions were found as follows:

Grade	No. of Examinations	Percentage of Positive Reactions
First	2,717	21.8
Second	2,106	31.2
Third	1,707	41.4
Fourth	1,325	46.6
Fifth	945	48.0

Of 395 girls given radiographic and clinical examinations 14 (3.5%) had active tuberculosis and 9 (2.3%) had old lesions; of 487 boys 16 (3.3%) had active tuberculosis and 6 (1.25%) had old lesions. Living standards of these children were excellent in two, good in four, fair in nine, poor in six, and very poor in nine. Tuberculosis infection is high among primary school children of Bursa City. At the 11th National Medical Congress, Prof. Nusret Karasu, of the department of phthisiology at Ankara University, reported that tuberculosis infection among primary school children in Turkey is 1.25 to 4.85%.

Antibiotics in Ophthalmology.—In *Göz Klinigi,* the Istanbul periodical for ophthalmology, volume 11, Dr. Nuri Fehmi Ayberk, medical director of the Istanbul-Haydar Pasha General Hospital and chief of the department of ophthalmology, reported his observations concerning antibiotics, anticoagulants, sulfonamides, cortisone, and tissue therapy in ophthalmology. Very good results have been obtained with streptomycin. While a 28-year-old man was under treatment for lung tuberculosis at a sanatorium a solitary tuberculum, the size of a pea, developed in his left eye. The patient was given 20 gm. of streptomycin, and the tuberculum gradually decreased and completely disappeared after a month. Tuberculous meningitis was thus forestalled. In a 30-year-old woman who had previously had spondylitis a tumor developed, the size of an almond, over the bulbar conjunctiva of the left eye. Biopsy revealed uveal lesions and the origin of the tumor to be tuberculosis. The patient was given 15 gm. of streptomycin, and the tumor decreased.

During the trachoma campaign work in the southeastern provinces excellent results were obtained with oxytetracycline (Terramycin). Subjective and objective amelioration resulted in from five to six days in patients with acute and complicated trachoma. Secondary infections, pain, and prolific aqueous humor decreased, and follicular hypertrophy of the conjunctiva diminished, but the trachoma virus did not completely disappear.

In 20 patients excellent results have been obtained with cortisone. A 19-year-old woman had parenchymatous keratitis in the left eye and vision of 1/10; her Wassermann and Kahn tests gave 3+ reactions. The patient was given 1 drop of a 1% cortisone solution three times a day for 10 days, the keratitis disappeared, and vision reverted to 8/10. A 28-year-old man had parenchymatous keratitis in the right eye, vision of 1/10, and a Wassermann test reaction of 3+. After 10 days of therapy with a 1% cortisone solution of one drop three times a day, the corneal infiltration subsided and vision became 5/10. This therapy in both patients was followed by penicillin and bismuth therapy. A 26-year-old man with iritis of undetermined origin in both eyes and negative Pirquet and Wassermann reactions recovered completely after 10 days of cortisone therapy; his vision became 9/10. A 47-year-old woman had subacute hypertensive iritis and lesions in both eyes; her right eye vision was 1/20 and her left eye 5/10. After 15 days of cortisone therapy vision of the right eye was 2/10 and that of the left eye was normal.

In purulent cases very good results have been obtained with penicillin. Of his many such cases Dr. Ayberk cites two. A 14-year-old boy had a furuncle of 15 days' duration over the brow of the left eye, edema then occurred. On admission to the hospital the boy was unconscious, at times he became excited, and he had a temperature of 40 C. The left eyelid and left side of the face were swollen and inflamed; examination revealed chemotic bulbar conjunctiva and exophthalmos of the left eye; the cerebrospinal fluid was cloudy and the pressure was 50 mm. of water; the Pandy test reaction was 4+, and the albumin and cells had increased. A diagnosis of cavernous sinus thrombophlebitis was made. The patient was given 800,000 units of penicillin for five days. The temperature reverted to normal; the patient's general condition improved; and infiltration, inflammation, and edema completely subsided. A 25-year-old woman had a severe headache accompanied by loss of vision in both eyes 20 days prior to admission to the hospital. Clinical and laboratory investigations revealed an optochiasmatic arachnoid. The pupils of both eyes were edematous. The patient, refusing an operation, was given 1 million units of penicillin for 10 days, with the result that the patient, who on admission could discern movement of fingers only at 10 cm., had attained a vision of 6/10, and the patient insisted on being discharged. When she returned three months later vision had reverted to its former low level. The patient again refused surgical intervention. There was no chiasmatic inflammation, but the optic nerve had become atrophic; so the second series of penicillin therapy did not benefit the patient. Penicillin has proved to be a valuable adjunct in the therapy of ophthalmologic diseases. Formerly purulent infections resulted in blindness in 15 to 20%, but the sulfonamides and penicillin have reduced it to 0.5%.

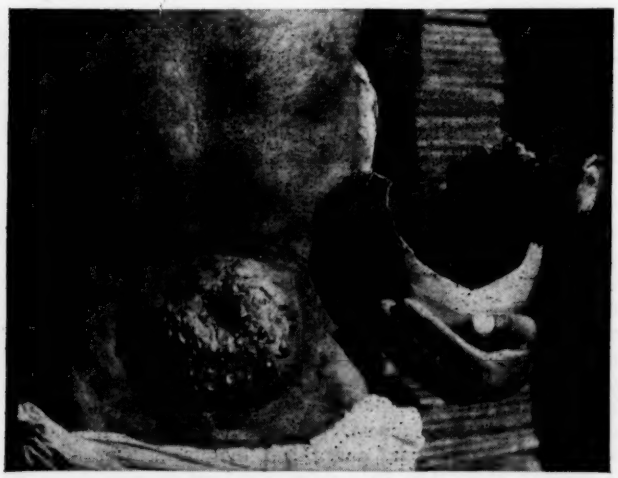
Fifteen patients with hypertension were given heparin or bishydroxycoumarin therapy. Dr. Ayberk cites the following cases: A 40-year-old woman with hypertension of 19/11 suddenly lost vision in the left eye five days prior to admission. Examination revealed thromboangiitis obliterans of the venae centralis retinae. The patient was given heparín, 150 mg. intravenously, daily for one week. Vision soon improved. After 15 days the patient attained a vision of 7/10. A 48-year-old bookbinder, while at work, suddenly lost complete vision in the right eye. Examination at the hospital a few hours later revealed hypertension of 20/12 and thromboangiitis obliterans of the venae centralis retinae in the right eye, he could see the movements of fingers a few centimeters away only. The patient was given heparin, 100 mg. intravenously. On the sixth day the patient had 6/10 vision. A 63-year-old patient with the same diagnosis and 19/10 hypertension was given 100 mg. of heparin intravenously for six days and attained a vision of 6/10. Formerly such patients were doomed to blindness. With anticoagulants, antibiotics, sulfonamides, cortisone, and tissue therapy it can now be forestalled. More than 30 patients, men and woman, 20 to 40 years old, who had retinitis pigmentosa, many of whom had night blindness, and who had vision of 1/10 to 1/50, were given placental grafts and had their vision restored to from 4/10 to 9/10. Patients who had retinopathy also benefited greatly by placental graft therapy.

CORRESPONDENCE

HOME TREATMENT

To the Editor:—One sees some unusual and amusing things in India. One afternoon a 32-year-old Caucasian (East Indian) man walked into the Giffard Mission Hospital. The mouth of a brass pot (a chimboo) was very firmly fixed to his anterior abdominal wall; in fact, a portion of the wall was inside the pot.

The patient had had a stomach-ache and had asked a neighbor's advice as to treatment. The neighbor advised that he take a chimboo (a round, 6-inch, brass pot with a 2-inch mouth), fill it half full of fresh cow dung, heat this well, and then put the mouth of the pot against his abdomen where the pain was. This, the neighbor said, would draw out the pain.



This sounded sensible to the man, so he proceeded to do it. After the pot had been in place for an hour or so, he tried to remove it, but it would not come off. He pulled; some of his friends pulled; but still the pot would not come off. After some thought they came to the conclusion that a vacuum inside the pot was holding it so tightly in place; therefore, if they went to the goldsmith and had him punch a hole in the bottom of the pot, the vacuum would be broken and the pot would surely come off. The goldsmith punched quite a liberal hole in the bottom of the pot, but still it would not come off.

The group then decided that the man should go to the Giffard Mission Hospital. A not-too-serious consultation was held, and the conclusion was reached that we should operate. We borrowed a pair of side-cutting pliers from the business manager and then cut away the pot. The appearance of the abdomen after removal of the pot can be seen in the second illustration. The paraumbilical area was edematous and greatly thickened. When the patient was trying to pull it out through the narrow neck of the pot it was the same as trying to pull a mushroom through a wedding ring. The abdominal wall was badly burned (second degree) from the hot contents of the pot. The patient stayed in the hospital for 10 days while the area healed. During that time he did not complain of abdominal pain so we assume that his home treatment was quite effective.

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HYDROCORTISONE (COMPOUND F) FREE ALCOHOL OINTMENT

To the Editor:—In a recent article in THE JOURNAL (**151**:468 [Feb. 7] 1953), we reported that the topical application of hydrocortisone acetate ointment was of value in the treatment of particular diseases of the skin. Our conclusions were drawn after comparing the effects of hydrocortisone acetate in various ointments applied to the affected areas of one side of the body with the effects of the respective ointment base, without hydrocortisone acetate, applied as a control to symmetrically situated affected sites. Observations on 62 patients were included in our first report.

Because oral administration of the free alcohol is more effective than administration of hydrocortisone acetate, we thought it important that ointments incorporating the free alcohol be compared with ointments containing the acetate. The clinical evaluation of the therapeutic effectiveness of the hydrocortisone free alcohol ointment was accomplished by comparing it with the hydrocortisone acetate ointment (incorporated in the same base and in equal concentration) used on the contralateral affected sites of the same patient. Forty patients with various dermatoses were studied. In 17, the hydrocortisone free alcohol ointment proved to be slightly more beneficial than the hydrocortisone acetate ointment. In 18, the hydrocortisone free alcohol and the hydrocortisone acetate ointments were of equal benefit. In the remaining five, the response was slightly better to the hydrocortisone acetate than to the free alcohol ointment. Our comparisons indicate that the clinical benefits from the topical use of ointments containing hydrocortisone free alcohol in selected dermatoses are, to say the very least, equal to those obtained from the use of hydrocortisone acetate ointments. This may be of practical significance if hydrocortisone free alcohol becomes available.

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COUNCIL ON MEDICAL SERVICE

The Council on Medical Service has prepared the following review of the Research Council's study because of the widespread interest in data concerning prolonged illness.

SURVEY OF PROLONGED NONOCCUPATIONAL ILLNESS BY RESEARCH COUNCIL FOR ECONOMIC SECURITY

This study is based on the hypothesis, as set forth by the Research Council for Economic Security, Chicago, that whenever and wherever illness strikes, it is costly.[1] When the illness is serious and endures for months or, for that matter, several weeks, it can be catastrophic economically for the person and his family. How frequently such prolonged illnesses occur, how many people are affected, how great the financial cost is, and how well the cost is being met are part of the data that are not available. Nevertheless, the presumed frequency and extent of prolonged illness have been and are being used in arguments both for and against such proposals as the extension of employee benefit plans, compulsory sickness compensation, and national health insurance. Facts are essential for the discussion and development of these programs and for the consideration of alternatives.

This is the first of several surveys that the research council has under consideration, and it will be confined to prolonged nonoccupational illnesses among employed persons. The council has as its ultimate expectancy comparable studies of related areas, such as dependents, the aged, and the self-employed. The current study covers a vital segment of the population, namely, the wage earner.

The objective of this survey is to establish ". . . the relation of the incidence and duration of prolonged illness to: (1) the different occupational groups; (2) the different income groups; (3) age; (4) sex; (5) the various types of employee benefit plans and the coverages or services available under these plans; (6) the medical facilities and health services within the employing establishment; (7) the availability and use of medical facilities in the community."

BASIS OF STUDY

This study is confined to all employed persons with so-called "prolonged illness," i. e., nonoccupational disabilities (sickness and accidents) that cause absences from work for more than four weeks. Sickness within the meaning of this study is defined as both nonoccupational illnesses and injuries not covered under workmen's compensation; normal pregnancy cases are not included. Any abnormality or complication that requires special medical care and absence from employment will be treated as an illness and will be included in this survey.

When completed, the study will cover the experiences of 400,000 employees, or 1% of all private nonagricultural employment (total—39,404,000).[2] Quotas have been assigned to each of the nine census regions, including metropolitan, urban, and semirural communities, and to industries classified as (1) mining, (2) construction, (3) manufacturing, (4) transportation and public utilities, (5) trade, (6) finance, and (7) service. Occupational classifications include (1) managerial and supervisory, (2) clerical, sales and kindred workers, (3) skilled, and (4) semiskilled and unskilled.

FACT-FINDING PROCEDURES AND EXHIBITS

This survey is a continuous study, "recording experience at the time an illness is terminated, during the course of a 12 month period. Negotiations must be carried on separately with each participating company to arrange for the installation of the study, the setting up of the procedures and for the training of personnel."

Incident to the survey requirements that data are to be assembled on a current basis and that a running record is to be kept for 12 months, four separate work sheets have been set up and identified as schedules A, B, C, and D. The first three schedules are prepared from company records, and the fourth is designed as an employee questionnaire.

Schedule A is a quarterly report to the council and includes (1) number of employees, (2) number of employees absent because of illness, (3) breakdown of absences because of illness, and (4) number of days absent. Schedule B is a report that will be made only once giving details of the medical care program, such as (1) medical personnel, (2) diagnostic aids, (3) medical service, and (4) outside arrangements including any formal arrangements that either supplement or are in lieu of company's own facilities and that are being used for the care of nonoccupational illnesses of employees, and details of the employee benefit plan provisions for (1) hospitalization, (2) surgical care, (3) medical care, (4) sickness compensation, and (5) paid sick leave. Schedule C is a quarterly report to council and includes (1) personal data, (2) a chronological record of the illness, (3) nature of the illness or accident, and (4) medical costs and group plan benefits. Schedule D is an employee questionnaire that covers information not usually available in company or claim record files. Such data are medical insurance in addition to the group plan at the company, source of funds to help pay for cost of illness, and type and cost of medical aid, including physician, nurse, prescriptions, and special equipment.

The scope of this survey anticipates the accumulation of a large volume of case material and a vast number of statistical correlations. The final result should, however, establish a valid base on which to evaluate the medical, social, and economic implications from prolonged nonoccupational illnesses among employed persons.

FIRST PROGRESS REPORT

The council reports that as of the middle of May, 1953, arrangements were completed for reports to be submitted covering the experience of some 202,000 employees (approximately 50% of the total quota).

The following statistical results are based on assembled data covering a continuous three month period for a total of 39,675 employees. Whether or not ratios resulting from statistical correlations of one-tenth of the total number to be studied are sufficiently valid to establish trends is a question that must be deferred. This small group does not represent a cross section of the full sample, and many of the resulting ratios may change completely when the experiences are recorded for a full 12 month period and when the data for the full sample of 400,000 persons are assembled.

A review of the number of absences showed that there were nine prolonged absences per 1,000 employees: If this were projected for the 12 month period, there would be 36 prolonged absences in that period. The council suggests that preliminary investigations indicate a projection of 40 or more prolonged absences per year. Whereas it was expected that the absenteeism rate among women would be considerably higher than among men, there were no marked differences in the ratios; in fact, the absentee incidence among women was slightly lower. Although the absenteeism rate for women may be higher for illnesses of short duration, it apparently may not be so with respect to prolonged illnesses. There was a wide variation between the absences of male supervisors and those

1. Survey of Prolonged Non-Occupational Illness Among Employed Persons; Nature, Extent and Economic Aspects, Publication No. 90, and Prolonged Non-Occupational Illness; First Progress Report, Publication No. 95, Chicago, Research Council for Economic Security, 1952.

2. Employees in Non-Agricultural Establishments, January, 1952, United States Department of Labor, Bureau of Labor Statistics, United States Government Printing Office, 1952. Government establishments have been excluded from total.

of male skilled workers, although there is some doubt as to the validity of the figures for supervisors. The number of prolonged absences for the supervisors is under "2" while for the skilled worker it was "15." These figures suggest that the skilled worker group may constitute a special problem area and that a special investigation may be necessary. "The nine absences represented a loss of 460 actual work days per 1,000 employees. This is equivalent to the loss of seven people full time for the three months period. The 460 days represent an average loss among the employees who were ill of 10 weeks of work (assuming a normal five-day work week)."

There were insufficient data on absences of less than one week to include the factor of the relation of prolonged absences to all absences in this report. Accordingly, comparisons were made between absences of one week or more and prolonged illnesses. Among all the workers covered in this report, 20% of all recorded absences of one week or more were prolonged illnesses. Here again women have an absence figure lower than the men, less than 15% compared to over 20%, respectively. "That the prolonged illnesses among skilled workers may present a special problem is re-emphasized. All of the other occupational groups are at or below the percentage for the whole group (20%) whereas the skilled worker showed an index figure of 48%."

The reversal of the incidence of absenteeism among female workers compared to male workers approaches confirmation in this group. Among male workers, prolonged illness accounted for 22% of all the absences; among the female workers, prolonged illness represented 13.4% of the absences. The research council suggests that, if prolonged illnesses represent 20% of all absences of one week or more, it is an important problem and that it becomes one of serious concern when it is noted that the prolonged illnesses were responsible for 56% of all the time lost during these absences.

Absences of not more than eight weeks represented 60% of the total absences but caused only 34% of the total time lost. Illnesses causing absences of more than 13 weeks, representing 20% of the illnesses, accounted for 46% of all time lost. The average duration of the prolonged illnesses (250 cases) was 51.18 days. While 250 illnesses are insufficient for any conclusions, they may be a clue. The duration figure is important in determining proper insurance coverage.

"Male and female workers were responsible for the same share of the prolonged illnesses as their percentage of the total number of employees. Clerical workers representing 17 per cent of all workers reported accounted for 11.45 per cent of all prolonged illnesses; an index figure of 33. Again male skilled workers representing less than 13 per cent of the workers reported accounted for 21 per cent of all of the prolonged illnesses; an index figure of 65."

The following ratios are based on 335 cases in which there was absence of more than four weeks. Some of the more obvious causes of prolonged illnesses were heart disease, nervous and mental disease, and chronic arthritis and rheumatism. It is interesting to note that, among the employees covered in this report, the largest percentage of cases were caused by diseases of the digestive system (29% of all cases). Diseases of the respiratory system caused 14.1%; fractures of the skull, spine, ribs, or limbs, 8.1%; malignant and benign neoplasms, 5.1%; and arthritis and rheumatism, except rheumatic fever, 4.8%. While diseases of the digestive system and respiratory tract were highest in terms of frequency, they were lowest in mean duration in weeks, 8.2 weeks and 7.7 weeks, respectively. Neoplasms and arthritis and rheumatism, which reflected the lowest percentage in frequency, were among the highest in terms of mean duration, 11.8 weeks and 13.6 weeks, respectively.

The data of the distribution of illnesses by age groups are, we believe, of sufficient interest to show that part of the chart reflecting "all illnesses" without any detailed consideration to that part of the chart breaking down the age groups according to disease.

Age Group	Number of Persons	%
24 and under	22	6.6
25-34	65	19.4
35-44	79	23.6
45-54	74	22.1
55-64	84	25.1
65 and over	11	3.2

There is only a 1.5 percentage point differential between the 35 to 44 age group and the 45 to 54 age group; the higher count is accounted for by the younger age group. With the exception of the group 24 years and under and the group 65 and over, the percentage point differential is not dramatic. If the preliminary ratio of 3.2% for the age group 65 and over is at all typical rather than atypical, prolonged illness may no longer be considered as being primarily a problem of geriatrics. "In only two of the disease groups did the workers over 45 account for more than one-half of the cases."

Half of the workers had been with their employer eight or more years. Approximately 17% had been employed less than 30 months, only 10% less than 19 months. Of the 335 employee samples, 59.3% had annual incomes of less than $3,500. Of this group, 21% had illnesses causing absences of more than 13 weeks. The council observes that, although the rate of incidence in this income group may not be any higher than that in any other, this represents the largest group of workers and the one least able to meet the cost.

SUMMARY

The ratios established in this preliminary report are based on only a small segment of the total sample, and, even with respect to this group, the total of desirable evidence has not been correlated. Accordingly, any indicated trends may prove to be more apparent than real. In spite, however, of the possible illusory aspects of the evidence before us, there are certain clues that legitimately stimulate our interest and attention. There is an apparent reversal of the absentee incidence among women workers compared to men. While the incidence of absenteeism among women is higher for illnesses of short duration, the ratio is apparently reversed for prolonged illness. Prolonged illness among skilled workers is emphasized and reemphasized to a degree that, if confirmed, will indicate a special investigation in this area. If prolonged illnesses prove to represent 20% of all absences of one week or more and are responsible too for approximately 56% of all time lost during these absences, then prolonged illnesses become a very important problem. If the average duration of some 250 illnesses (51.18 days each) is at all typical, prolonged illness becomes an important factor in terms of appropriate insurance coverage. On the basis of disease classification, diseases of the digestive system occur most frequently, and neoplasms (malignant and benign) and arthritis and rheumatism are the fourth and fifth, respectively, in order of frequency. The more apparent disabilities, such as heart diseases and nervous and mental diseases, are not even included in "the largest percentage of cases." Thus early diagnosis and adequate initial care may contribute to immediate improvements in incidence and duration. The low incidence in the age group 65 and over may necessitate a readjustment of the relative importance of geriatrics in the treatment of prolonged illnesses. The income group that can least afford it (annual incomes of less than $3,500) accounted for 59.3% of the prolonged illnesses.

Certainly the study to date has provided sufficient data, irrespective of the probable ratio adjustments, to indicate that we should look with interest toward the final correlations based on the total sample of 400,000 wage earners. The completed study should give to all interested valid data with which to attack the important problem of prolonged nonoccupational illness among the wage earners of this country.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Am. J. Diseases Children, Chicago

85:393-522 (April) 1953

Use of Cortisone and Corticotropin (ACTH) in Treatment of Reticuloendotheliosis in Children. M. H. Bass, S. O. Sapin and H. L. Hodes.—p. 393.
Angiocardiography in Congenital Heart Disease Correlated with Clinical and Autopsy Findings. B. M. Gasul, H. Weiss, R. F. Dillon and others.—p. 404.
*Measles Encephalomyelitis. M. J. Fox, J. F. Kuzma and J. D. Stuhler.—p. 444.
Nephrotic Syndrome in Children: Observations on Clinical Course and Influence of Sulfonamide and Antibiotic Therapy. I. Philips, J. K. Calvin and B. M. Kagan.—p. 451.
Effect of Hemopoietic and Other Agents on Hydroxyphenyluria of Premature Infants. H. M. Nitowsky, C. D. Govan Jr. and H. H. Gordon.—p. 462.

Measles Encephalomyelitis.—Seventy-seven patients with measles encephalomyelitis were treated at a Milwaukee hospital from 1926 to 1951. The ages of the patients ranged from 5 months to 32 years, but nearly two-thirds were between the ages of 4 and 7. The onset of encephalomyelitis varied from several hours to nine days after the appearance of the morbilliform rash, but in nearly half of the cases it began three to four days after the appearance of the rash. A total of 22 of the patients died, and 15 of these had coma or convulsions or both. The cell count of the spinal fluid varied, but in nearly three-fourths of the patients it was below 90. Although it was over 90 in about half of those who died, the authors do not believe that the cell count of the spinal fluid is of prognostic significance. The protein content of the spinal fluid was increased in 61% of the patients, and the sugar content of the spinal fluid was normal or above normal in all but two of the patients. The leukocyte counts of the blood varied greatly, but in 60% of the patients it was between 9,000 and 18,000. Thirty-six of the 55 survivors answered a follow-up questionnaire, which revealed that 22 had completely recovered; one had choreiform movements for one year with frequent headaches, dizzy spells, and vomiting since that time; one has had persistent tremors involving the extremities; one is epileptic; one has a residual cord bladder, foot drop, and myopia; one is poorly coordinated; three are mentally defective; and six have shown personality changes. The results of necropsy studies on five of the patients are reported. The treatment of measles encephalomyelitis is largely symptomatic. In commenting on the diagnosis, the authors say that a diminished or absent cough reflex was one of the earliest signs of measles encephalomyelitis. It was noted in 74% of the patients. No medication containing codeine should ever be given to depress the cough of measles. The authors have observed patients with codeine intoxication who were hospitalized because of a supposed measles encephalomyelitis with convulsions, lethargy, vomiting, nuchal rigidity, cyanosis, and elevation of temperature. In each instance the spinal fluid findings were normal, and the patient recovered completely within 24 hours after oxygen and helium therapy was instituted.

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Titles marked with an asterisk (*) are abstracted.

A.M.A. Arch. Ind. Hyg. & Occupat. Med., Chicago

7:275-366 (April) 1953

Rapid Determination of Lead in Old Urine Samples. M. O. Amdur.—p. 277.
Comparative Toxicity of Synthetic and Natural Glycerin. C. H. Hine, H. H. Anderson, H. D. Moon and others.—p. 282.
Observations on Toxicity of Aldrin: 1. Growth and Estrus in Rats. W. L. Ball, K. Kay and J. W. Sinclair.—p. 292.
*Acute Toxicity of Carnotite Ore Dust. H. B. Wilson, H. E. Stokinger and G. E. Sylvester.—p. 301.
Toxicity of Butyl Stearate, Dibutyl Sebacate, Dibutyl Phthalate, and Methoxyethyl Oleate. C. C. Smith.—p. 310.
Blood and Urine Changes in Experimental Beryllium Poisoning. C. J. Spiegl, L. LaFrance and B. J. Ashworth.—p. 319.
Planning a Study to Determine Effects of Air Pollution on Health: Review of Methodology. A. F. W. Peart and G. H. Josie.—p. 326.
Anthracosilicosis Occurring in Foundry Employee. L. E. Hamlin.—p. 339.

Acute Toxicity of Carnotite Ore Dust.—Uranium miners are exposed to the dust from carnotite ore in their work. To determine the toxicity of this material the authors exposed animals to carnotite ore dust dispersed in a chamber atmosphere. Mean daily dust concentration was approximately 84 mg. per cubic meter; the average mass median diameter of the chamber dust (particle size) was 1.39 μ. Rabbits and one goat were exposed for 131 exposure hours during 31 calendar days; rats were exposed for 137 exposure hours during 32 calendar days. Ninety-two per cent of the rabbits died; 10% of the rats died. The goat survived. Toxicity was further evidenced in the rabbits by weight loss, by sharp elevation of blood nonprotein nitrogen and urinary protein levels, and by renal tubular damage; in the rat by weight loss, by renal tubular damage, and by gross lung damage; and in the goat by renal tubular damage. Mean deposits of uranium and vanadium in the rat lungs (370 and 146 μg per gram of fresh tissue, respectively) were 50 to 300 times as great as corresponding amounts in the femur and kidney. The same was true for uranium in the tissues of rabbits and the goat. Deposits of uranium and vanadium in the rat lungs increased linearly with exposure hours. The only hematological finding of interest was basophilic stippling in two of the rabbits. From the results of this experiment the authors conclude that carnotite ore dust inhaled by animals under the conditions of this experiment is highly toxic to the rabbit, moderately toxic to the rat, and slightly toxic to the goat. The toxicity is characteristic of uranium poisoning and in degree closely resembles that of uranium trioxide.

A.M.A. Arch. Internal Medicine, Chicago

91:417-576 (April) 1953

*Hydralazine (Apresoline®) Hydrochloride: Pharmacological Observations and Clinical Results in Therapy of Hypertension. J. H. Moyer.—p. 419.
*Pneumococcic Meningitis: Study of 102 Cases. J. D. Alexander Jr., H. F. Flippin and G. M. Eisenberg.—p. 440.
Intermittent Bundle-Branch Block: Observations with Special Reference to Critical Heart Rate. M. A. Shearn and D. A. Rytand.—p. 448.
Influence of Long-Term Bishydroxycoumarin (Dicumarol) Therapy on Liver Function. M. L. Meitus and P. Wasserman.—p. 464.
Serum Mucoprotein Level in Differentiation of Hepatogenic from Obstructive Jaundice. E. M. Greenspan and D. A. Dreiling.—p. 474.
*Cortisone in Treatment of Shoulder-Hand Syndrome Following Acute Myocardial Infarction. H. I. Russek, A. S. Russek, A. A. Doerner and B. L. Zohman.—p. 487.
Syphilis: Review of Recent Literature. H. Beerman, I. L. Schamberg, L. Nicholas and L. Katzenstein.—p. 493.
Hepatolenticular Degeneration: Review of Literature and Report of Case with Dimercaprol (BAL) Therapy. M. M. Schechter and C. A. Jones.—p. 541.

Hydralazine (Apresoline) Hydrochloride in Hypertension.—Moyer discusses the results obtained in the treatment of ambulatory patients with rather severe hypertension using hydralazine alone, or in conjunction with ganglionic blockade with hexamethonium. The dose employed was 25 to 50 mg. four times daily. Nineteen of 54 patients treated with hydralazine obtained an initial reduction in mean blood pressure of more than 20 mm. that was maintained for three months or

more. After one year only nine patients continued to take the drug, and only five of these nine continued to maintain a significant reduction in mean blood pressure (excess of 20 mm., or below 150 mm. systolic and 100 mm. diastolic). In the remaining four side-reactions occurred when the drug is given in doses that will reduce the blood pressure. Eleven of 20 patients had proved unresponsive to hexamethonium alone in gradually increasing doses beginning with 250 mg. four times daily. In nine a significant blood pressure reduction was obtained with hexamethonium alone, but it was felt that better stability and/or additional reduction could be obtained with combined hexamethonium and hydralazine therapy. After hydralazine was added to the hexamethonium regimen, no significant reduction in blood pressure occurred in 7 of the 11 patients who failed to respond to hexamethonium alone, but 4 did show a significant response to combined therapy. In seven of the nine patients who had obtained some response to hexamethonium alone, there was a significant additional response when hydralazine was added, but in the two others there was no additional response. Of 32 patients who had proved unresponsive to hydralazine alone all but six showed a significant reduction in blood pressure following the administration of hexamethonium. Hydralazine, apparently reduces the blood pressure through a central vasodepressor action. At the same time it stimulates (centrally) the sympathetic nerves to the heart, causing tachycardia and increased cardiac output. During continued oral therapy the cardiac stimulant effect is lost long before the hypotensive effect. Eventually tolerance to the hypotensive response also develops. The cardiac stimulant effect is blocked off if hexamethonium has been given in amounts adequate to produce ganglionic blockade. Hydralazine reinforces the hypotensive effect of hexamethonium. Although hydralazine increases renal blood flow in patients with and without renal damage, glomerular filtration is not increased. The combined use of hexamethonium and hydralazine may produce a dramatic and sudden reduction in blood pressure, which in the presence of severe renal damage may be associated with a significant reduction in glomerular filtration rate and renal excretory function. Therefore, careful evaluation of changes in renal excretory function by repeated blood urea nitrogen determinations is necessary when treating hypertensive patients who have renal damage.

Pneumococcic Meningitis.—Alexander and associates review 102 cases of pneumococcic meningitis seen at the Philadelphia General Hospital during the past decade. Autopsy records were available in 68. Factors influencing the mortality rate were studied. The prognosis for recovery was more favorable in the 1 to 15-year-old group than in other age groups. The mortality rate does not appear significantly influenced by the presence of bacteremia or coma, but the rate is significantly higher when the meningitis is secondary to pneumonia than when the sinuses, middle ear, mastoid, or head trauma are involved. Pneumococci of types 4 and 12 were found in a significantly greater number of cases and were associated with a greater number of deaths than other types. Penicillin alone, or penicillin in combination with sulfonamides, is more effective in reducing the mortality rate than are sulfonamides alone or the sulfonamides in combination with type-specific anti-pneumococcus serum. The efficacy of penicillin is probably influenced by the speed with which therapy is begun and the intensity of the therapy. Intrathecal administration of penicillin does not seem necessary when moderate intramuscular doses of penicillin (800,000 to 2,400,000 units) and oral doses of sulfonamides (4 to 6 gm.) are given daily, or massive doses of penicillin (1,000,000 units every two hours) are administered intramuscularly. The rationale for the combined therapy is the demonstrated synergistic activity of penicillin and the sulfonamides against the pneumococcus. The rationale for the massive penicillin therapy is the ability to establish penicillin concentrations in the cerebrospinal fluid that are inhibitory for the pneumococcus. In view of the encouraging results obtained with these therapeutic schedules, surgical intervention should be confined to cases in which the response is not as anticipated.

Cortisone in Shoulder-Hand Syndrome Following Myocardial Infarction.—Cortisone was employed in the treatment of 17 patients in whom the shoulder-hand syndrome developed as a complication of acute myocardial infarction. In all these patients previous treatment with physical therapy, manipulative therapy, or local and stellate ganglion blocks was without significant effect. Cortisone produced complete relief of signs and symptoms in five patients, marked improvement in eight, moderate improvement in three, and no significant response in one. The striking feature of the treatment was its dramatic effect in the relief of pain, often within 24 to 48 hours. In addition, there was concomitant but often less marked improvement in the range of motion at affected joints. Vasomotor disturbances were also rapidly influenced, with decrease or disappearance of edema and improvement in temperature, color, and sudomotor activity of the hand. In patients responding favorably, there was no recurrence of symptoms after discontinuance of treatment. No thromboembolic complications were encountered in this series. These and previous observations fail to confirm the serious risk of vascular complications that is claimed to result from the use of this drug. Cortisone appears to be a safe and extremely effective form of treatment in refractory cases of the shoulder-hand syndrome complicating acute myocardial infarction.

A.M.A. Arch. Neurology and Psychiatry, Chicago

69:415-550 (April) 1953

Psychotic Reactions in Problem Drinkers Treated with Disulfiram (Antabuse). E. A. Macklin, A. Simon and G. H. Crook.—p. 415.
Visual Disturbances as Result of Nystagmus on Direct Forward Gaze: Effect of Amobarbital (Amytal®) Sodium. M. Nathanson, P. S. Bergman and M. B. Bender.—p. 427.
Intellectual Functions in Myxedema. R. M. Reitan.—p. 436.
Symptoms and Signs Referable to Basal Ganglia in Brain Tumor. D. Sciarra and B. E. Sprofkin.—p. 450.
Endogenous Eosinopenia in Institutionalized Patients with Mental Deficiency. F. Halberg, R. Engel, A. E. Treloar and R. J. Gully.—p. 462.
Study of Adrenocortical Physiology in Normal and Schizophrenic Men. H. Hoagland, G. Pincus, F. Elmadjian and others.—p. 470.
Subdural Hematoma Following Subarachnoid Hemorrhage. J. Golden, G. L. Odom and B. Woodhall.—p. 486.
Pain from Dermal, Periosteal, and Fascial Endings and from Inflammation: Electrophysiological Study Employing Differential Nerve Blocks. W. Landau and G. H. Bishop.—p. 490.
An Extralemniscal Sensory System in Brain. J. D. French, M. Verzeano and H. W. Magoun.—p. 505.
A Neural Basis of Anesthetic State. J. D. French, M. Verzeano and H. W. Magoun.—p. 519.

A.M.A. Arch. Ophthalmology, Chicago

49:375-480 (April) 1953

Electroretinographic Studies in Cases of Pigmentary Degeneration. J. Jacobson and J. M. O'Brien.—p. 375.
Bilateral Superior Oblique Paralysis. M. J. Urist.—p. 382.
Honeycomb Colloid Degeneration of the Retina. M. G. Alper and J. A. Alfano.—p. 392.
Hydrocortisone (Compound F) in Ophthalmology: Clinical and Experimental Studies. P. R. McDonald, I. H. Leopold, A. W. Vogel and R. D. Mulberger.—p. 400.
*Treatment of Chemical Burns of the Eye. R. D. Harley.—p. 413.
Miotic Therapy of Chronic Glaucoma—Changing Trends. K. C. Swan.—p. 419.
Clinical Testing of Visual Acuity. H. Ehlers.—p. 431.
Fundus Photographs in Color Using a High-Speed Flash Tube in Zeiss Retinal Camera. K. N. Ogle and C. W. Rucker.—p. 435.
Aqueous Veins: Their Status Eleven Years After Their Detection. K. W. Ascher.—p. 438.
Lens and Vitreous. J. G. Bellows.—p. 452.

Treatment of Chemical Burns of the Eye.—Kuhn, who treated over 300 cases of chemical and thermal burns of the eye with calsulfhydryl (Hydrosulfosol), reported that pain was controlled, healing was more rapid, visual restoration was accelerated, permanent disability was reduced, and there were fewer indications for conjunctival flaps. Calsulfhydryl has also been reported to be a valuable adjunct in the treatment of ocular injuries caused by anhydrides and detergents. To verify those reports Harley studied the effects of calsulfhydryl in a total of 157 rabbit eyes in which burns had been produced with various chemical agents, including strong acids, strong alkalis, anhydrides, and specific agents designed for enzyme inhibition. In 53 pairs of rabbit eyes in which corneal lesions were produced with various chemicals, results showed that the

calsulfhydryl-treated eye was neither better nor worse than the control, untreated eye. With only one chemical, iodoacetate, did calsulfhydryl, in three paired experiments, give consistently better results than those in the control eye. This was to be expected, since calsulfhydryl supplies sulfhydryl radicles, which combine with iodoacetate, thus preventing iodoacetate from inhibiting tissue enzymes and denaturing tissue protein. The author feels that the chief sphere of activity for sulfhydryl compounds is in lesions produced by specific enzyme-inhibiting agents that combine chemically with the sulfhydryl radical. Studies of lesions caused by specific chemicals should be undertaken for further evaluation of this compound. Present day concepts of the treatment of ocular burns are outlined and modified in the light of the observations described. The technique of "denudation of the cornea" advocated by McLaughlin has certain advantages, especially in alkali burns. Cortisone appears to be of definite value in inhibiting fibroblastic proliferation and corneal vascularization.

Alabama State Medical Assn. Journal, Montgomery

22:255-278 (April) 1953

Management of Emphysema. L. L. Friedman.—p. 255.
Infectious Mononucleosis with Acute Thrombocytopenic Purpura: Report of Case. W. L. Smith.—p. 257.
Intramedullary Nailing of Femoral Fractures. C. H. Wilson, C. L. Yelton and D. G. Vesely.—p. 261.
*Hypersensitivity to Protamide: Report of Case. A. S. Zdanis.—p. 267.

Hypersensitivity to Protamide.—Protamide, a proteolytic enzyme prepared from hog stomach, has been in use for over 10 years in the treatment of tabes dorsalis, because of its ability to relieve the lightning pains of tabes in a high percentage of cases. Lately, this drug has been used in the control of the pain and itching occurring in herpes zoster. In the case of herpes zoster presented here there occurred a severe systemic reaction immediately following the injection of the recommended dose of protamide. Skin tests performed later seemed to indicate a hypersensitivity in comparison with the results in six other persons. It is evident that this drug should be used with caution. A fraction of the original dose should be given at first, in order to reduce the severity of the reaction if one should occur.

American Journal of Clinical Pathology, Baltimore

23:311-412 (April) 1953

*Excretion and Distribution of Polyvinyl Pyrrolidone in Man: As Determined by Use of Radiocarbon as Tracer. R. K. Loeffler and J. Scudder.—p. 311.
Isoagglutinin Response to Injections of Specific Substances A and B: Derived from Animal Sources and from Meconium. G. R. Sickles and P. P. Murdick.—p. 322.
Tetrazolium Salts: New Tool in General and Experimental Pathology. M. M. Black, B. W. Zweifach and F. D. Speer.—p. 332.
Regranulation of Beta Cells of Islets of Langerhans Following Insulin and Starvation. S. T. Nerenberg.—p. 340.
Effect of Plasma in Toxemia of Pregnancy on Volume of Normal Erythrocytes. Y. M. Bromberg and S. Z. Rosenberg.—p. 343.
Infestation of Skin with Demodex Folliculorum. R. L. Breckenridge.—p. 348.
*Cytomegalic Inclusion Pneumonitis in Adult. J. P. Wyatt, T. Simon, M. L. Trumbull and M. Evans.—p. 353.
Human Infection with Atypical Acid-Fast Organisms: Report of Two Cases with Pathologic Findings. V. B. Buhler and A. Pollak.—p. 363.

Excretion of Polyvinyl Pyrrolidone.—The excretion rate and the subsequent distribution in the body of retained portions of the proposed plasma extender polyvinyl pyrrolidone were studied in four patients with advanced cancer who required hydration by the intravenous route. Determinations were made by using C^{14} labeled polyvinyl pyrrolidone (PVP-macrose) as a tracer. About one-third was excreted in the urine in the first six hours, one-half in the first 12 hours, and about two-thirds in the first 24 hours. Small amounts were excreted in the feces. Each of the four patients died within from two to eight days following the administration of polyvinyl pyrrolidone, and necropsies were performed on all. The unexcreted portion of polyvinyl pyrrolidone showed a distribution consistent with that of any inert material of large molecular size, with the greatest concentrations tending to occur in the kidneys, lungs, liver, spleen, and lymph nodes. No histological evidence of polyvinyl pyrrolidone itself, or damage caused by it, was demonstrated. The authors emphasize that nothing can be concluded from these data about the effectiveness of polyvinyl pyrrolidone-macrose as a plasma extender or about possible physiological damage resulting from its use.

Inclusion Pneumonitis in Adult.—The occurrence of severe and distinctive pneumonitis due to the salivary gland virus is reported in a 54-year-old woman and in a 28-year-old man. Biopsy of the lung permitted the diagnosis to be made during life. Histopathological examination of lungs in both cases revealed essentially similar features. The lung parenchyma was greatly altered. The cells lining the alveoli were large and prominent, varying from cuboid to swollen polyhedral forms with round vesicular nuclei. This reversion to a "fetal type" of lining cell was prominent in all areas. Many of these cells were exfoliated into the alveoli or lined up around the septal walls, and showed both giant nuclear inclusions and multiple cytoplasmic inclusions. All the alveoli were distended by large plugs of esosinophilic protein coagulum with only threads of fibrin that stained blue with Weigert's stain. Plastered against the septal walls and spreading through pores of Cohn were dense membranes, which stained intensely with Sudan black B and periodic acid (Schiff) and metachromatically with toluidine blue. The inflammatory cells, observed principally in the septal walls, were numerous and predominantly of the large mononuclear or plasma cell variety. The mononuclear infiltrate and the hyaline membrane suggested a virus infection. The alveolar walls were greatly widened by fluid and nodal collections of monocytic cells. Frank intra-alveolar hemorrhage was focal but extensive in distribution. In the male patient, the mononuclear response was so intense that it simulated a lymphomatous infiltration; in addition a necrotizing arteritis was observed, the cause of which is obscure. It is suggested that the fulminating salivary-gland-virus disease in adults may result from altered susceptibility induced by the action of antimetabolites.

American J. Digestive Diseases, Fort Wayne, Ind.

20:91-116 (April) 1953

Superficial Cancer of Gastric Mucosa. G. E. Konjetzny.—p. 91.
Problem of Acute Abdominal Pain. H. Gauss.—p. 96.
Investigation of Enteric Infections in Caribbean Area: I. Survey of Intestinal Parasitism in Lombardia, Michoacan, Mexico. M. P. Natt, A. Lopez-Rico and V. M. Young.—p. 105.
Treatment of Migraine, Gout and Heberden's Nodes: (Factor Common to These Conditions). M. B. Levin and B. A. Gwynn.—p. 107.
Biological Basis of an Alimentary Regime Preventing Intestinal Fermentation and Intoxication. N. Dobrovolskaia-Zavadskaia.—p. 109.

American Journal of Medicine, New York

14:389-536 (April) 1953

Biochemical Disturbances and Clinical Symptoms During Prolonged Exchange Resin Therapy in Congestive Heart Failure. L. Greenman, J. B. Shaler and T. S. Danowski.—p. 391.
Metabolic Studies on Effects of Ion Exchange Resins in Edematous Patients with Cardiac and Renal Disease. R. E. Weston, J. Grossman, E. R. Borun and others.—p. 404.
Treatment of Edema by Removal of Body Sodium by Cation Exchange Resin. L. E. Duncan Jr.—p. 425.
Heparin Treatment of Angina Pectoris. A. Grüner, T. Hilden, F. Raaschou and H. Vogelius.—p. 433.
*Effect of Heparin in Effort Angina. S. H. Rinzler, J. Travell, H. Bakst and others.—p. 438.
Edema of Acute Nephritis. J. P. Peters.—p. 448.
Differential Diagnosis, Pathogenesis and Treatment of Thrombocytopenic Purpuras. E. L. Lozner.—p. 459.

Effect of Heparin in Effort Angina.—Graham discovered that angina pectoris is sometimes relieved during heparin therapy while he was investigating the effects of heparin on the concentration of the serum lipoproteins (S_f 12-20 and 20-100). The efficacy of heparin in effort angina has since been corroborated by some and denied by others. Rinzler and coworkers report observations on 18 patients with unequivocal evidence of coronary artery disease and with a history of chest pain produced by effort (usually walking) and relieved promptly by rest or nitroglycerin. The patients were observed for approximately two months prior to heparin administration. To eliminate the factor of unconscious bias the double blind-

fold method was employed. This meant that the study was conducted by a team, and that not merely the patient but also the physicians who questioned and examined them, injected the solutions, and later assessed the data were unaware of the nature of the coded solution given to any particular patient. The patients were paired with respect to age, sex, duration of effort angina, and incidence of myocardial infarction, and were then divided at random into two parallel series. Heparin was administered to one group of nine patients while the placebo was given concurrently to the other group of nine twice weekly over a period of eight to nine weeks. Each dose of heparin was 100 mg. The effect of the injections on effort angina was judged by the daily report card system (the patient's day-to-day evaluation of cardiac pain) and by the average number of nitroglycerin tablets used per week. Electrocardiograms and ballistocardiograms were taken before and after the course of injections. The results, based on the analysis of 1,883 report card days recorded by 18 patients, show that heparin has no greater effect than a placebo in the control of effort angina. A comparison of the levels of serum lipoproteins of the S_f 12-20 and S_f 20-100 classes showed no significant change in concentration after six weeks of heparin or placebo therapy. Side-effects consisted of dizziness and headache; their incidence was slightly higher in the placebo than in the heparin group.

American Journal of Ophthalmology, Chicago

36:433-598 (April) 1953

Type of Congenital Ocular Motor Apraxia Presenting Jerky Head Movements: Jackson Memorial Lecture. D. G. Cogan.—p. 433.
*Evaluation of Urethane of Beta-Methylcholine Chloride in Chronic Glaucoma. F. Frisch and I. H. Leopold.—p. 442.
*Present Status of Goniotomy. O. Barkan.—p. 445.
Cataracts in Galactosemia: Observations in Three Cases. A. Patz.—p. 453.
Posterior Half-Incision of Cornea for Astigmatism: Operative Procedures and Results of the Improved Tangent Method. T. Sato.—p. 462.
Management of Eye Casualties in Far East Command During Korean Conflict. F. E. Hull.—p. 467.
Effect on Ocular Bacterial Flora of Local Treatment with Chloromycetin (Chloramphenicol), Terramycin or Penicillin-Streptomycin Ophthalmic Ointments in Preoperative Cataract Cases and Miscellaneous Infections. D. Locatcher-Khorazo.—p. 475.
Bacterial Sensitivity Tests in Treatment of Chronic External Ocular Infections. J. A. McNeill.—p. 480.
Etiology of Acute Glaucoma. B. Rosengren.—p. 488.
Pupil in Syphilis. N. S. Jaffe.—p. 493.
Effect of Age on Carbonic Anhydrase Activity of Bovine Lenses. T. Reich and R. W. Healy.—p. 500.
Machek Operation Applied to Lower Lid for Relief of Senile Extropion. J. E. Lebensohn.—p. 504.

Bethanechol Chloride in Chronic Glaucoma.—The urethane of bethanechol (Urecholine) chloride is a cholinergic agent simulating acetylcholine in its action, but it is not as rapidly destroyed by cholinesterase. It combines the two components that individually render methacholine (Mecholyl) and carbachal (Doryl) more stable than acetylcholine in tissues. It is possibly the longest acting miotic and the most potent of this choline series. Even in dilute solutions, it can be autoclaved at 120 C for 20 minutes without loss of potency. Its use in ophthalmology has been limited, but it has been used widely in postoperative urinary retention, abdominal distention, gastric retention, and megacolon. Because of its potential value in the medical therapy of glaucoma, it was tried by Frisch and Leopold in treatment of chronic glaucoma. Comparisons were made with other cholinergic agents, namely, both the nitrate and hydrochloride salts of pilocarpine, carbachol, and physostigmine, an anticholinesterase. Bethanechol chloride was tried also in several cases of glaucoma secondary to venous thrombosis and in several cases of absolute glaucoma. The concentration of the drug employed was 1% in benzalkonium (Zephiran) (1:10,000). It was applied by the instillation method, as were the other drugs with which it was compared. The authors conclude that in a 1% concentration this drug approximates pilocarpine (1 or 2%) and carbachol (0.75%) in the treatment of chronic noncongestive glaucoma. In the 1% concentration the drug was not effective in glaucoma secondary to venous occlusion. The authors list the following disadvantages of this drug: It caused a mild allergic reaction in one of 42 eyes. There is the possibility of bronchoconstriction in asthmatic persons, but no instance of this occurred in this series, and ciliary spasm may occur but it is not marked. The drug appears to be an effective and safe miotic that may possibly be useful as a substitute for pilocarpine or carbachol in chronic glaucoma.

Present Status of Goniotomy.—Barkan believes that goniotomy is indicated in all bilateral and unilateral cases of congenital glaucoma in which increased pressure is the result of obstruction of the angle by persistent embryonic tissue or false anterior insertion of the iris, provided that Schlemm's canal has not been obliterated by prolonged distention of the globe. This includes the majority of cases of congenital glaucoma. A total of 178 eyes with congenital glaucoma were subjected to goniotomy between 1936 and 1952. The results of the operations on the first 76 eyes were previously reported. Goniotomy preserved useful vision in most of the 178 eyes with infantile glaucoma. In 129 eyes pressure was normalized and vision maintained or restored. In those cases in which the diagnosis was made early, the operation insured vision sufficient to permit the child to attend ordinary schools. The operation was unsuccessful in 26 eyes. In the last three years, by virtue of improvements and simplifications in technique, it has been possible to operate with the glass under gonioscopic control on eyes in which this procedure would formerly have been impossible. This technique is described. A case of glaucoma associated with aniridia was operated on successfully by goniotomy. While no conclusion can be drawn from an isolated case, the author feels that the good result in this case encourages the hope that goniotomy may in the future prove effective in similar cases. The author pleads for the early diagnosis of congenital glaucoma and for prompt, adequate operation by goniotomy. The operation should be performed under gonioscopic control whenever possible. If, soon after its onset, increased intraocular pressure is normalized by goniotomy, transparency of the cornea is almost completely restored and maintained, and vision is afforded an opportunity to develop. The urgency of prompt relief of the increased pressure is stressed.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

69:539-722 (April) 1953

New Objective of American Radium Society: Scientific Study of Physical Properties and Therapeutic Application of all Pertinent Ionizing Radiations. H. F. Hare.—p. 539.
Significance of Growth in Roentgenological Skeletal Changes in Early Congenital Syphilis. A. Engeset, S. Eek and O. Gilje.—p. 542.
Roentgenography of Kerosene Poisoning (Chemical Pneumonitis). J. Gershon-Cohen, L. S. Bringhurst and R. N. Byrne.—p. 557.
Paraduodenal Hernias. P. B. Parsons.—p. 563.
Pseudodiverticular Sarcoma of the Stomach. A. B. Skorneck.—p. 590.
Primary Chondrosarcoma of Occipital Bone. S. Krantz and B. B. Gay Jr.—p. 598.
Lipoma of Corpus Callosum: Case Report. C. D. Smith and E. N. Weaver.—p. 605.
Leukemia and Pregnancy, with Case Report. F. H. Lutze.—p. 608.
Chordoma: Its Roentgen Diagnostic Aspects and Its Response to Roentgen Therapy. E. J. Sennett.—p. 613.
*High Energy Electrons for Treatment of Extensive Superficial Malignant Lesions. W. W. Evans, J. H. Anson, H. F. Hare and others.—p. 623.
Observations on Series of Aryl Triiodo Alkanoic Acid Derivatives with Particular Reference to New Cholecystographic Medium, Telepaque. J. O. Hoppe and S. Archer.—p. 630.
Simple Method of Roentgen Pelvimetry. R. W. Curry.—p. 638.
Satisfactory Copies from Original Roentgenograms on Production Basis. H. G. Morse.—p. 647.

High Energy Electrons for Superficial Malignant Lesions.—There has been an increasing interest in the possibility of using artificially accelerated high energy electrons in radiation therapy. It has been recognized that the biological effect of high energy cathode rays and roentgen rays should be similar, since the ionization that they produce in tissue is mostly the result of electron interaction. Similar doses of electrons and roentgen rays were required to elicit a specific biological response in micro-organisms. The superiority of cathode rays for the treatment of superficial malignancies arises from the unique localization of its ionizing energy below the absorbing surface. The authors compare the distribution obtained with 2.5 mev. cathode rays with that of 100 kv. roentgen rays with standard factors of filter and distance used in superficial therapy. The dosage distribution in depth obtained from a radioactive stron-

tium (Sr^{90}) beta ray source using a typical surface applicator is also shown. So far only four patients have been treated with the cathode rays, which were produced by an electrostatic accelerator of the Van de Graaff type insulated with compressed gas designed at the Massachusetts Institute of Technology. These patients had extensive skin lesions no longer amenable to other forms of treatment, including roentgen therapy. Two of the four patients had pathologically and clinically diagnosed mycosis fungoides and two atopic dermatitis. Blood studies carried out during treatment revealed no changes indicative of damage to the hematopoietic system. In the two patients with mycosis fungoides most lesions entirely disappeared, and, at the time of writing, their skin, while still pigmented as a result of disease, appeared normal. The two patients with atopic dermatitis improved only slightly. The authors feel that cathode rays will be efficacious in the therapy of a number of benign skin lesions, including keloids, verrucae, industrial dermatoses, and tinea capitis. Cathode rays should be helpful in the treatment of localized malignant lesions, such as basal cells and squamous cell carcinoma. They appear to be especially applicable to generalized superficial malignant lesions such as mycosis fungoides.

American Journal of Surgery, New York

85:469-588 (April) 1953

Perinephric Abscess. R. S. Hotchkiss.—p. 471.
Küntscher Nailing of Forearm in Problem Cases. J. E. M. Thomson, D. A. Willander and E. S. Maxim.—p. 486.
Intramedullary Fixation of Fractures of Forearm: Evaluation of 20 Successive Unselected Cases. R. C. Robertson.—p. 496.
Radical Surgery for Cancer of Extremities. A. G. James and W. Furste. —p. 503.
Carcinoma of Breast. J. L. Donhauser.—p. 513.
Carcinoma of Penis: Evaluation of Recurrence Following Limited Surgery and Presentation of an Extended Surgical Attack. P. B. Hudson, J. A. Hopkins and G. W. Fish.—p. 519.
Management of Benign Lesions of Lower Bowel: New Technic Utilizing the Electrotome. G. S. Rost.—p. 523.
Malignant Tumors Originating in Meckel's Diverticulum: Case Report of a Leiomyosarcoma and Review of Literature. F. A. Hill and D. E. Janelli.—p. 525.
Evaluation of Vascular Ligations in Reversing Experimental Ascites. N. C. Jefferson and H. Necheles.—p. 529.
Intrathoracic Hürthle Cell (Oxyphil Cell) Tumor of the Thyroid. W. Sinclair Jr. and B. B. Larsen.—p. 534.
Trichlorethylene Anesthesia in Pediatric Urology. H. I. Roseman.—p. 539.
Modified Twin Stitch Technic for Urinary Incontinence. R. Tauber. —p. 541.
Effects of Early and Late Ambulation Upon the Surgical Patient. L. T. Palumbo, H. H. Samberg, R. E. Paul and others.—p. 544.
Box Top Closure for Huge Incisional Hernia. L. V. Rush and H. L. Rush. —p. 552.

Am. Practitioner & Digest of Treatment, Philadelphia

4:247-304 (April) 1953

Medical Management of the Poliomyelitis Problem. R. Batson.—p. 247.
Psychiatric Aspects of Menopause. W. Karliner.—p. 256.
Pituitary Influence on Growth and Development. R. Klein.—p. 261.
*Raynaud's Disease and Raynaud's Phenomenon. A. L. Scherbel.—p. 266.

Raynaud's Disease and Raynaud's Phenomenon.—Raynaud's phenomenon, a functional vasospastic disorder, is frequently a manifestation of serious systemic disease. It must be distinguished from Raynaud's disease proper, which is characterized by the following criteria established by Allen and Brown: (1) episodes of Raynaud's phenomenon excited by cold or emotion; (2) bilaterality of Raynaud's phenomenon; (3) absence of gangrene, or if present, its limitation to minimal grades of cutaneous gangrene; (4) absence of any primary disease that might be causal; and (5) persistence of symptoms for two years or longer. Since patients with Raynaud's disease have no serious organic vascular disease, they should be reassured. Progression of the disease is possible, however, and examination at regular intervals is advisable. The patient should be advised that the body, as well as the extremities, must be sufficiently warm. Since smoking produces vasoconstriction and reduces skin temperature, patients who smoke excessively should be advised to abstain. Conservative therapy is sufficient if the disease is mild and nonprogressive; sympathectomy is the most satisfactory treatment if symptoms increase in severity or complications develop. Discussing the conditions that may be associated with secondary Raynaud's phenomenon, the author mentions among others: thromboangiitis obliterans, arteriosclerosis obliterans, pneumatic hammer disease, generalized scleroderma, periarteritis nodosa, and conditions resulting from various traumas, such as gun-shot wounds, fractures, severe sprains, and bruising injuries near large blood vessels. Occasionally a cervical rib or the shoulder-hand syndrome are associated with neurovascular symptoms. Diseases of the nervous system that may be complicated by secondary Raynaud's phenomenon are anterior poliomyelitis, progressive muscular atrophy, myelodysplasia, spina bifida, spinal cord tumors, protruded intervertebral disks, and head injuries. Arsenic intoxication may also be associated with secondary Raynaud's phenomenon. Whenever Raynaud's phenomenon is secondary to some other disease, treatment should be directed against the underlying disease.

American Review of Tuberculosis, New York

67:401-552 (April) 1953. **Partial Index**

*Late Results of Modified Bed Rest in Active Uncomplicated Minimal Pulmonary Tuberculosis. R. S. Mitchell.—p. 401.
*Late Results of Treatment of Primary Tuberculous Pleurisy with Effusion with Modified Bed Rest. R. S. Mitchell.—p. 421.
Personality Characteristics of Tuberculous Patients who Leave Tuberculosis Hospital Against Medical Advice. M. E. Rorabaugh and G. Guthrie.—p. 432.
Role of Lymphatics in Development of Bronchogenic Tuberculosis. P. Schwartz.—p. 440.
Pulmonary Histoplasmosis: Study of 22 Cases with Identification of H. Capsulatum in Resected Lesions. T. F. Puckett.—p. 453.
Coexisting Pulmonary Coccidioidomycosis and Tuberculosis. H. F. Stein. —p. 477.
Mode of Action of Isoniazid. W. R. Barclay, R. H. Ebert and D. Koch-Weser.—p. 490.
Clinical Evaluation of Hemagglutination Reaction. A. G. Hollander, M. Frobisher Jr. and K. Kalisch.—p. 497.
Influence of Various Sources of Nitrogen on Activity of Antimicrobial Drugs: II. Mycobacterium Avium. E. D. Weinberg.—p. 503.
*Control Study of Comparative Efficacy of Isoniazid, Streptomycin-Isoniazid, and Streptomycin—Para-Aminosalicylic Acid in Pulmonary Tuberculosis Therapy: III. Report on 28-Week Observations on 649 Patients with Streptomycin Susceptible Infections. F. W. Mount and S. H. Ferebee.—p. 539.

Bed Rest in Minimal Pulmonary Tuberculosis.—From 1927 through 1946, 589 patients with active, uncomplicated minimal tuberculosis were treated by modified bed rest alone at Trudeau Sanatorium, New York; they were followed for 5 to 25 years. On this regimen the patient spent approximately 20 to 21 hours per day reclining in bed or on a chaise longue, eating meals in an adjoining room, and had full bathroom privileges. Because the mortality due to tuberculosis was quite low (5% in 20 years), rates of progression of tuberculosis were used to measure the effectiveness of the treatment. The term "progression" is defined as any definite increase of disease or development of cavity interpreted from the chest roentgenogram. Each search for a possible correlation of the rates of progression and various factors such as age, sex, extent of disease, was first made by using "five-year progression (any) rates." The "five-year progression (any) rate" was the proportion of patients having at least one progression, as defined, during residence at the sanatorium or during the first five years after discharge. Since contact with 26 of the 589 patients was lost in less than five years after discharge, only 563 remained available for analysis by this method. Of these 563 patients, 201 (35.8%) at the end of the 20 year follow-up have had at least one known progression. The condition of 154 (27.6%) progressed at some time during the 20 years to advanced disease, i. e., beyond the minimal classification. The chance of recurrent progression among those who had a primary progression was approximately the same as the chance of a first progression in the entire group. The age of the patient and the extent of the disease were observed to be related to the incidence of later progression. Sex, location of disease, duration of modified bed rest, duration of sanatorium residence, and duration of time away from full employment had no demonstrable relationship to later progression. Despite the low tuberculosis mortality, progressions and recurrent progressions of minimal tuberculosis produced a total loss of economic usefulness of sufficient magnitude to justify a continued search for a more dependable form of treatment for minimal tuberculosis than modified bed rest.

Bed Rest in Tuberculous Pleurisy with Effusion.—In 194 cases of primary tuberculous pleurisy with effusion, with and without minimal pulmonary infiltration, treatment consisted of modified bed rest at the Trudeau Sanatorium, New York. The patients were followed for 5 to 25 years after discharge. Of the 194 patients, 10 died of tuberculosis, a cumulative tuberculosis mortality of 5% in 20 years; the cumulative rate of reactivation of tuberculosis was 23.7% within the same period. Most of the initial reactivations of tuberculosis occurred within five years following discharge. Contact was lost with 27 (14%) of the 194 patients. Of the remaining 167 patients, 142 (85%) were well and able to work 5 to 25 years after discharge. Evidence suggested that the presence and extent of minimal pulmonary infiltration is related to the rate of reactivation of tuberculosis during the first five years after discharge. Other factors, which were apparently unrelated to the incidence of reactivation of tuberculosis, were as follows: age, sex, severity of symptoms, presence or absence of Mycobacterium tuberculosis in sputum and pleural fluid, and duration of modified bed rest and sanatorium residence.

Comparison of Isoniazid, Streptomycin and Isoniazid, and Streptomycin and *p*-Aminosalicylic Acid in Pulmonary Tuberculosis.—Of 649 patients with pulmonary tuberculosis susceptible to streptomycin who were treated and observed for 28 weeks, 203 were given 1 gm. of streptomycin twice weekly plus 10 to 12 gm. of *p*-aminosalicylic acid daily; 219 received 1 gm. of streptomycin twice weekly plus 150 to 300 mg. of isoniazid daily; the remaining 227 patients received 150 to 300 mg. of isoniazid alone daily. Thirteen of the 649 patients died during the 28 weeks of observation: three from the streptomycin-*p*-aminosalicylic acid group, two from the isoniazid group, and four from the streptomycin-isoniazid group died of tuberculosis, while three in the last-named group died of myocardial infarction, and one of cerebral hemorrhage. Improvement, as evidenced by roentgenographic, clinical and laboratory findings, continued with all three treatment regimens. At the end of 28 weeks, 47% of the patients in the streptomycin and *p*-aminosalicylic acid group, 54% of those in the streptomycin and isoniazid group, and 51% of the patients in the isoniazid group demonstrated at least a moderate degree of roentgenographic improvement; approximately an additional 25% showed slight improvement. Thus the results of treatment were essentially similar on the three regimens.

American Surgeon, Atlanta, Ga.

19:313-396 (April) 1953

Malignant Melanoma. J. P. McNeill, J. V. Goode and A. Caroe. —p. 313.
*Problem of Wound Disruption. H. M. Schiebel and B. Creech.—p. 318.
New Technic of Combining Thoracoplasty with Pulmonary Resection. W. F. Stone Jr.—p. 326.
Thoracoabdominal Approach to Upper Abdomen. H. Acuff and J. H. Hall.—p. 335.
Use of New Long Lasting Local Anesthetic Solution for Relief of Pain After Thoracoplasty and Pulmonary Resection. W. R. Deaton Jr. —p. 349.
Technical Safeguards in Partial Gastric Resection. J. M. Parker—p. 354.
Surgical Treatment of Surface Lesions of Head and Neck. C. E. Lockhart.—p. 361.
Conservative Treatment of Hydronephrosis. H. S. Browne.—p. 370.
Unilateral Lobotomy for Treatment of Intractable Anxiety States. E. H. Parsons, R. D. Woolsey, S. R. Banet and G. H. Lawrence.—p. 374.
Management of Common Anorectal Conditions with Special Emphasis on Prevention of Pain. R. H. Bell.—p. 382.
Staged Resection for Pelvic Colon and Rectum with Secondary Anastomosis. G. E. Gruenfeld.—p. 386.

Wound Disruption.—After reviewing the physiology of wound healing, Schiebel and Creech discuss the etiological factors in disruption, emphasizing that delayed wound healing and increase in intra-abdominal pressure postoperatively are the most important of these factors. They review the records of 23 cases seen in a community hospital of 225 beds over a period of 10 years. The operations were performed by several surgeons, but the technique of wound closure was usually the same, with the use of continuous surgical catgut in the peritoneum and interrupted sutures of cotton or silk in the fascial layer. Disruption followed cholecystectomy in five cases, appendectomy in three cases, and malignant lesions were present in three cases. Anemia was present in two cases and obesity in one. Intestinal obstruction and/or abdominal distention complicated eight cases. Retching or postoperative coughing was a definite factor in causing disruption in eight cases. There were two operations on the colon. Infection was not important. When dehiscence is discovered, any eviscerated bowel should be covered with a sterile dressing and the abdomen taped to prevent further disruption. Morphine is given and a gastric suction tube is inserted. The stomach is aspirated and the tube is left in place. Dextrose is given intravenously. If indicated before or during operation, transfusions of whole blood are given. If the patient's condition permits, the wound is resutured at once. In the 23 cases observed at their own hospital, closure of the wound on the day of disruption seemed to have no influence on the mortality, since all five patients who died had been treated in this way. The mortality rate is highest after colon operations and in patients with cancer. The chief causes of death are pneumonia and peritonitis, but pulmonary and myocardial infarction are found in some patients who come to autopsy.

Angiology, Baltimore

4:103-182 (April) 1953

*Treatment of Peripheral Vascular Diseases with Cyclospasmol: (Mandelic Acid Ester of 3, 5, 5-Trimethylcyclohexanol). T. W. van Wijk.—p. 103.
Pedunculated Thrombus of Left Auricle Causing Death During Aortic Embolectomy. S. H. Gumbiner and J. L. Keeley.—p. 114.
Treatment of Post-Poliomyelitic Ulcerations of Legs with Lumbar Sympathectomy. F. Martorell, T. Alonso and V. Salleras.—p. 118.
Lipogram Studies in Coronary Atherosclerosis: I. Response to Lipotropic Agents. L. M. Morrison.—p. 123.
Serum Phospholipid-Cholesterol Ratios in Coronary Atherosclerosis: II. Response to Lipotropic Agents. L. M. Morrison.—p. 130.
Clinical Plethysmography: Part I: An Improved Direct Writing Plethysmograph. T. Winsor.—p. 134.
Id.: Part II: Plethysmographic Procedures of Clinical Importance. T. Winsor.—p. 149.
Action of Beta-Pyridil Carbinol (Roniacol) on Peripheral Circulation of Normal Persons and in Certain Pathologic States. C. M. Castro and L. de Soldati.—p. 165.

Cyclospasmol in Peripheral Vascular Disease.—A new vasodilator drug, Cyclospasmol (the 3, 5, 5-trimethylcyclohexanol ester of mandelic acid) was given a therapeutic trial over 12 to 18 months in 33 men and 17 women between the ages of 16 and 76. Of the 50 patients, 28 had arteriosclerosis obliterans, 5 had thromboangiitis obliterans, and 17 had various vasospastic disturbances. The drug was administered orally, starting with an initial dose of 100 to 200 mg. daily, while subsequently doses up to 600 to 1,000 mg. were given in advanced cases. No toxic or important undesirable side-effects were observed, even after prolonged administration. Of the 28 patients with arteriosclerosis obliterans, 17 (61%) obtained good results and 7 (25%) moderate results; and 4 (2 of whom had familial hypercholesterinemia) were therapeutic failures. Three of the five patients with thromboangiitis obliterans obtained good results, one was moderately improved, and one was a therapeutic failure. Eight of the 17 patients with vasospastic disturbances had excellent results, 4 were moderately improved, and 5 were therapeutic failures. The criteria of success were not only the clinical course but also objective symptoms, such as claudication time, healing of extensive gangrenous lesions, and skin temperature. The angina pectoris that was frequently associated with arteriosclerosis obliterans seemed to be favorably influenced by Cyclospasmol. During six months various patients with angina pectoris were, therefore, given alternately placebo tablets, 300 to 600 mg. of Cyclospasmol, 100 to 300 mg. of crystalline visammin (khellin), and combined Cyclospasmol and visammin tablets (one tablet containing 50 mg. of Cyclospasmol and 25 mg. of visammin three times daily). The combined tablets caused disappearance or a considerable decrease of anginal symptoms, but the treatment has been too short to warrant definite conclusions. As a result of his experience, the author states that Cyclospasmol is a valuable asset in the treatment of peripheral vascular diseases.

Annals of Allergy, Minneapolis

11:137-266 (March-April) 1953

Microscopic Observations of Intrahepatic Circulation of Living Guinea Pigs Before and During Anaphylaxis. W. S. Burrage and J. W. Irwin. —p. 137.

Hypothyroidism in Pediatric Allergy. W. A. Reilly.—p. 143.

*Atopic Dermatitis Caused by Inhalant Antigens and its Immunologic Therapy. H. E. Diamond.—p. 146.

ACTH in Gelatin: Clinical Results with Repository Adrenocorticotropic Hormone in Allergic Diseases. S. J. Levin.—p. 157.

Persistence of Histaminic Responses in the Human During Cholinesterase Administration. R. D. Barnard, H. T. Stanton Jr. and B. Goldman. —p. 170.

Whole Pollen Antigen Hydrochloride. G. E. Rockwell.—p. 175.

Food-Induced, Allergic Musculoskeletal Syndromes. W. Kaufman.—p. 179

Pollen Survey of West Texas. V. E. Friedewald.—p. 185.

Ménière's Disease: Case Report and Discussion. G. R. Laub.—p. 190.

Hay Fever in Immigrants. H. H. Shilkret and L. C. Lazarowitz.—p. 194.

Drug Tolerance in Asthma: Fatal Salicylate Poisoning from Physiologic Dose. G. L. Waldbott, K. E. Blair and R. McKeever.—p. 199.

Use of Chlor-Trimeton Maleate® Injectable in Blood Transfusions. D. B. Frankel and N. Weidner.—p. 204.

Respiratory Acidosis—Pathogenesis and Treatment. M. S. Segal, M. J. Dulfano, J. A. Herschfus and J. A. Shanks.—p. 206.

Hypoallergic Penicillin V (Pyribenzamine-Penicillin): Comparison of Results and Final Conclusions from All Studies. S. W. Simon.—p. 218.

Dermatitis Caused by Inhalant Antigens.—In over 20 years of practice in allergy Diamond was frequently confronted with eczematous dermatoses of obscure allergy. In recent years he observed an increasing number of patients who presented themselves primarily for the treatment of atopic dermatitis, and many of them came on the recommendation of older patients with respiratory complaints whose concomitant dermatoses had responded to treatment with antigens involved in the respiratory disorders. Of 236 consecutive new patients seen by the author from January, 1949, to July, 1952, 179 complained primarily of respiratory tract symptoms. Among these, the diagnosis of a concomitant atopic dermatitis was made in 23 instances (9.5% of the total). In the remaining 57 patients of this series the primary complaint was dermatological; 23 of these patients had atopic dermatitis, and 7 of the 23 also had bronchial asthma, allergic rhinitis, or hay fever. The author presents case histories that illustrate the improvement of atopic dermatitis coincidentally with the immunologic treatment of hay fever, bronchial asthma, or allergic conjunctivitis. From slowly accumulating experiences the author deduced the following concepts: 1. A high incidence of eczematous dermatoses is seen among subjects with allergic respiratory disease, such as hay fever and bronchial asthma. 2. The dermatoses often improve coincidentally with the treatment of the respiratory complaints by means of individually adjusted and, as a rule, small, doses of extracts from the antigens involved in the respiratory disorder. 3. Exacerbations of dermatitis caused by inhalants are observed following the injection of extracts from dust, pollens, molds, etc., for the purpose of testing for therapy. 4. Favorable results are obtained in the treatment of such skin lesions with concentrations of dust, pollens, or mold extracts in much smaller doses than those used in the treatment of respiratory complaints.

Annals of Internal Medicine, Lancaster, Pa.

38:647-912 (April) 1953

*Management of Malignant Hypertension. M. Sokolow and M. F. Schottstaedt.—p. 647.

Malignant Hypertension Associated with Unilateral Renal Artery Occlusion: Three Cases. E. G. Laforet.—p. 667.

Necrotizing Renal Papillitis. J. S. Silberstein and J. T. Paugh.—p. 689.

Perforation of Interventricular Septum Following Myocardial Infarction. V. F. Bond Jr., C. R. Welfare, T. N. Lide and R. L. McMillan. —p. 706.

*Natural History of Lupus Erythematosus Disseminatus. R. A. Jessar, R. W. Lamont-Havers and C. Ragan.—p. 717.

"Pararheumatic" Arthropathies. H. H. Friedman, S. Schwartz, M. Trubek and O. Steinbrocker.—p. 732.

Essential Hyperlipemia. C. R. Joyner Jr.—p. 759.

*Common Type of Vertigo Relieved by Traction of Cervical Spine. D. Davis.—p. 778.

Splenectomy in Rheumatoid Arthritis. C. L. Steinberg.—p. 787.

Further Studies on Electrocerebral Dysfunction and Use of Anticonvulsants in Labile Diabetes. M. Fabrykant.—p. 814.

Management of Malignant Hypertension.—According to Sokolow and Schottstaedt, the prognosis of malignant hypertension is no longer hopeless, particularly if modern treatment is instituted prior to the stage of severe renal impairment. Treatment should be instituted promptly after adequate investigation has excluded the presence of reversible conditions such as pheochromocytoma and unilateral atrophic pyelonephritis. The most effective medical management at the present time appears to be the use of hexamethonium by parenteral injection, combined with the oral administration of hydralazine, low sodium diet, and adequate attention to the emotional needs of the patient. The newer veratrum alkaloids, such as protoveratrine, are also of value. An adequate trial of hexamethonium given subcutaneously by the authors to 17 patients with malignant hypertension resulted in reversal of papilledema and clinical improvement in 10, including 2 with chronic glomerulonephritis and 2 with chronic pyelonephritis; in these 4 patients the creatinine clearance rates were between 33 and 57 cc. per minute prior to therapy. In patients whose creatinine clearance rates were less than 30 cc. per minute, renal failure progressed despite hexamethonium therapy. There were two patients in whom the addition of 300 mg. daily of hydralazine administered orally to 70 mg. of hexamethonium twice daily subcutaneously was of striking benefit after only modest improvement resulted from parenterally administered hexamethonium. A combination of hexamethonium given orally and hydralazine orally may prove to be as effective as the combination suggested above, but, in view of the results reported by Kilpatrick and Smirk, this remains to be proved. The patient should be under close medical supervision, preferably in the hospital, when the treatment with the new antihypertensive agents is instituted, and great care should be exercised to avoid hypotensive reactions. Prior to January, 1950, bilateral radical lumbodorsal sympathectomies were performed by the authors on eight patients. In six of these patients reversal of papilledema occurred. Death in uremia occurred in only one patient, who had subacute glomerulonephritis. The other five deaths were due to cardiac or cerebral lesions. Two patients are living 43 and 57 months after diagnosis. Of four other patients with malignant hypertension on whom sympathectomies were performed after January, 1950, two who showed temporary improvement and reversal of papilledema died one year and 22 months, after the operation. The other two patients had reversal of papilledema and were alive and well 23 months and 6 months after the surgical intervention. It is apparent that sympathectomy in the early stages of malignant hypertension in patients with adequate renal function is an effective method of treatment; the accelerated phase of the disease is reversed in 30 to 50% of the patients.

Lupus Erythematosus Disseminatus.—In the past 15 years, 44 patients (group A) with lupus erythematosus disseminatus were observed at Columbia University College of Physicians and Surgeons and at the Presbyterian Hospital in New York and data of 279 additional patients (group B) were collected from the literature of 1948 to 1952. Female patients made up 98% of the first group and 85% of the second group. The age of onset varied from 5½ to 60 years in group A, but the peak incidence in both groups was in the second, third, and fourth decades, with an approximately equal distribution in each decade. Only 3 of the authors' 44 patients had a family history of rheumatic disease, while this feature was not evaluated in the cases collected from the literature. Arthritis and arthralgia were common and were noted in 77% of group A and in 68% of group B. Cardiac manifestations were seen frequently in both groups. Respiratory tract involvement was less frequently observed in both groups. Transient chest pain was a prominent complaint, though less frequently accompanied by objective findings. Generalized enlargement of lymph nodes was noted repeatedly in patients of both groups. Gastrointestinal complaints were prominent in 36% of the group A patients, and in a somewhat smaller percentage of the group B patients. Peripheral and facial edema was present more frequently in group A than in group B. Raynaud's phenomenon was observed in 16% of the group A patients, while the incidence of these changes in group B was low. Eyeground changes were infrequently noted in group B, but occurred in 9 (20%) of the 44 patients. Anemia was common and was fre-

quently apparent at the onset in both groups. Elevation of the erythrocyte sedimentation rate to more than 50 mm. in the first hour was present in 86% of the group A patients and in an approximately similar percentage of group B. Albuminuria of greater than 1+ was seen in 70% of the group A patients, and in 58% of group B. Electrocardiographic changes indicative of myocardial or pericardial disease were observed in both groups. Of the 44 group A patients, 31 died and 13 (30%) were alive more than five years after the onset of the disease; 22% of 103 patients who had been followed for more than five years were alive in group B. As a result of these observations, the authors state that, while the prognosis of lupus erythematosus disseminatus is unfavorable, approximately 22% of the patients remain alive for periods in excess of five years. At least 6 of the 44 patients have been relatively asymptomatic for periods ranging for from 4 to 20 years. This fact must be considered in an evaluation of a therapeutic regimen. Although the usefulness of corticotropin (ACTH) and cortisone in the palliative therapy of the patients with lupus erythematosus disseminatus cannot be denied, it will remain for further long-term studies to determine the effect of these hormones on the life spans of these patients.

Postural Vertigo Relieved by Traction of Cervical Spine.—In a reported group of 43 patients with chest pain as the chief complaint, a history of vertigo was elicited in 21. In some, this symptom had recurred over a period of years. Generally it was mild and transient, but in several it was severe and, at times, incapacitating. In addition to chest pain and vertigo, other manifestations, such as suboccipital headache, shoulder girdle pain, limitation of head rotation, spasm and tenderness of the posterior cervical muscles, and tenderness over the cervical or dorsal spine and in the parasternal region, were often present. Detailed reports are presented of seven patients between the ages of 38 and 70 years with vertigo as a major complaint. The most striking feature was the precipitation of the attack of vertigo by sudden turns of the head and neck from long-maintained positions, and almost regularly by the act of getting out of bed in the morning. The attacks of actual vertigo were usually of very short duration, lasting less than a minute and often only a few seconds, but they recurred frequently. After some bodily activity, such as dressing or walking, the tendency to recur was lessened. An unsteadiness of gait persisted in most instances a few minutes, in some for hours, and in a few for days. Nausea and occasionally vomiting accompanied the vertigo. In several instances attacks were reproduced by having the patient get up suddenly from the examining table. Most of these attacks were interrupted and recurrences prevented or lessened by cervical traction and exercises. The manual method in the reclining position and the overhead method of Hanfling were used. Evidence that this vertigo is of cervical origin may be summarized as follows: (1) the striking response to traction and exercises, as shown by the immediate effect on the attack itself and the prevention of recurrences; (2) the close relation of the attacks to a prolonged position of the cervical spine, the effect of sudden changes from this position, and the reduction of attacks after bodily activity has been resumed; (3) the high incidence of the other manifestations of the cervicodorsal radiculitis; and (4) the absence of clinical manifestations of intracranial disease, cerebral arteriosclerosis and disturbances of the labyrinth. The radicular distribution of changes in skin sensation in patients with shoulder girdle and chest pain in this condition suggests nerve root involvement, and a similar upper cervical mechanism may be assumed as the basis for the vertigo, which is effectively treated by appropriate orthopedic measures.

Arkansas Medical Society Journal, Fort Smith

49:193-212 (April) 1953

Ectopic Pregnancy: Analytical and Diagnostic Features. M. R. McCaskill, T. Trieber and E. T. Ellison.—p. 193.
Recent Advances of Present Trends in Cancer Treatment and Research Surgery. G. T. Pack.—p. 197.

Delaware State Medical Journal, Wilmington

25:77-102 (April) 1953

The Hernia Problem: Confessions and Impressions. J. C. Pierson.—p. 77.
Tissue Electrolyte Abnormalities in a Case of Chronic Congestive Heart Failure. R. A. Neubauer and J. W. Abbiss.—p. 80.
Treatment Complications in Case of Lymphatic Leukemia with Secondary Hemolytic Anemia. R. W. Frelick and O. Sluzar.—p. 83.
Breast Lesions: Review and Classification. R. M. Zwicker.—p. 88.
Cystadenocarcinoma of Ovary: 20 Years Survival After Known Peritoneal Metastases: Case Report. E. A. Mekanik.—p. 95.
Bronchogenic Carcinoma: Report of 149 Cases. E. Y. Gledhill.—p. 97.

Florida Medical Association Journal, Jacksonville

39:791-862 (May) 1953

Adams-Stokes Syndrome. S. Grau.—p. 811.
Rational and Scientific Method for Evaluating Fluid and Electrolyte Therapy Postoperatively. J. H. Kay and A. Ochsner.—p. 815.
Review of Effects of Various Drugs on Human Cerebral Circulation and Metabolism. P. Scheinberg.—p. 817.
Intramedullary Fixation of Fractures of Long Bones. J. T. Ellis and S. W. Windham.—p. 820.

Illinois Medical Journal, Chicago

103:197-260 (April) 1953

Endocrine Disorders in Office Practice. J. H. Hutton.—p. 235.
Obstetrical Hemorrhage. W. C. Scrivner.—p. 240.
Practical Office Gynecology. W. J. Reich and M. J. Nechtow.—p. 244.
*3-o-toloxy 1, 2 Propanediol as an Adjunct in Treatment of Drug Addiction. J. J. McLaughlin and L. S. Schlan.—p. 247.
Intussusception. W. F. Jacobs.—p. 250.

Treatment of Drug Addiction.—In a trial on 63 psychiatric patients it had been found that mephenesin (Tolserol) reduced or abolished gross tremor, relieved severe anxiety, and calmed hypomanic patients. In two drug addicts the new compound appeared to abolish the withdrawal symptoms. This report deals with observations on 20 drug addicts to whom the new drug was given as an adjunctive to alleviate or control some of the withdrawal symptoms. All of the addicts were men and used the drugs intravenously. All but one who used morphine were addicted to heroin, and some also, used cocaine. The 20 patients were divided in two groups: a group of 12 being given mephenesin as an adjunctive, and a group of 8 serving as controls and receiving no mephenesin. Methadone in decreasing amounts was substituted for the addictive drug in both groups. The initial dose of methadone varied from 10 to 30 mg. every four hours and depended upon the duration of addiction, amount of drug used, emotional stability, age, weight, and general physical condition of the patient. The optimal dose of mephenesin appeared to be 1 gm. every three hours. It was found that in patients receiving the adjunctive therapy withdrawal can be more rapid; muscle twitchings, cramps, and tremor can be controlled; and there is less anxiety. Patients are able to carry on a more normal existence, taking part in group activities and performing light physical duties; insomnia appears to be decreased. To be effective, however, the adjunctive treatment must be given early, before withdrawal symptoms appear.

Industrial Medicine and Surgery, Chicago

22:93-140 (March) 1953. **Partial Index**

Allergy and Occupational Diseases. E. Sidi, C. Albahary and R. Longueville.—p. 93.
Incidence of Respiratory Allergy as Disclosed in Survey of 37,497 Persons, 1949-1950. W. B. Blanton, E. C. Matthews, M. T. Tobin and S. E. Shanks.—p. 99.
Anomalies Versus Fractures. P. Thurber Jr.—p. 103.
Occupational Leukoderma, with Report of Cases. J. V. Klauder and J. M. Kimmich.—p. 106.
*Barbers' Disease. W. Waris.—p. 111.

Barbers' Disease.—Waris presents the histories of three barbers in whom a sinus developed in the web between two fingers. He lists data on these cases and eight others that had previously been described in the literature. Most of these sinuses, which in previous reports were usually referred to as "pilonidal" sinuses because they contained hair, were on the right hand. They were more commonly in the web between the third and fourth fingers and less often between the second and third or fourth and fifth fingers. Hair clippings sometimes

penetrate into the skin of the finger webs of barbers and cause a foreign body granuloma and cyst formation. A sinus of this kind containing short hairs may be quite harmless for many years before a secondary infection causes suppuration and surgical treatment is needed. These finger web sinuses are an occupational disease of barbers, but they are rather rare. It seems possible that the movements of the barber's fingers rub hair clippings into the finger web in such a way that the hair bores into the skin. Furthermore, the constant opening and shutting of the web may produce a negative pressure that promotes penetration of hair into the skin.

Journal of Applied Physiology, Washington, D. C.

5:471-566 (March) 1953. **Partial Index**

Oxygen Toxicity: Effects in Man of Oxygen Inhalation at 1 and 3.5 Atmospheres Upon Blood Gas Transport, Cerebral Circulation and Cerebral Metabolism. C. J. Lambertsen, R. H. Kough, D. Y. Cooper, G. L. Emmel and others.—p. 471.

Quantitation of Beat-to-Beat Changes in Stroke Volume from Aortic Pulse Contour in Man. H. R. Warner, H. J. C. Swan, D. C. Connolly and others.—p. 495.

Effects of Atropine on Heart Rate and Oxygen Intake in Working Man. S. Robinson, M. Pearcy, F. R. Brueckman and others.—p. 508.

Analysis of One-Stage Test for Prothrombin Time. C. A. Owen Jr. and J. L. Bollman.—p. 515.

Transcapillary Exchange Rates of Deuterium Oxide and Thiocyanate in Forearm of Man. E. D. Freis, T. F. Higgins and H. J. Morowitz. —p. 526.

Finger Numbness in Very Cold Winds. N. H. Mackworth.—p. 533.

Effects of Posture and of Neck Compression on Outputs of Water, Sodium and Creatinine. V. Netravisesh.—p. 544.

Ratio Between True and Apparent Creatinine in Sweat. D. E. Bass and I. T. Dobalian.—p. 555.

Method for Rapid Measurement of Skin Temperature During Exposure to Intense Thermal Radiation. J. D. Hardy.—p. 559.

5:567-645 (April) 1953

Biochemical and Hematologic Characteristics of Blood from Hepatic Portal Vein in Man. H. R. Bierman, L. P. White, K. H. Kelly and H. L. Steinbach.—p. 567.

Comparison of Effects of Certain Blood Alkalinizers and Glucose Upon Competitive Endurance Performance. W. R. Johnson and D. H. Black. —p. 577.

Relationship Between Mouth, Skin and Arterial Blood Temperature. G. H. Eurman and M. Mendlowitz.—p. 579.

Effect of Moderate Exercise on Electrocardiogram in Healthy Young and Middle-Aged Men. E. Simonson.—p. 584.

Age Changes in Maximum Conduction Velocity of Motor Fibers of Human Ulnar Nerves. A. H. Norris, N. W. Shock and I. H. Wagman. —p. 589.

Sweating Response to Local Heat Application. F. B. Benjamin.—p. 594.

Prevention of Airsickness Among Airborne Troops. H. I. Chinn, W. R. Gammon and M. E. Frantz.—p. 599.

Carbon Dioxide and Respiratory Regulation at Altitude. F. G. Hall. —p. 603.

Adaption to High Altitudes: Changes in Lung Volumes During First Seven Days at Mt. Evans, Colorado. S. M. Tenney, H. Rahn, R. C. Stroud and J. C. Mithoefer.—p. 607.

Obstructive Apnea in Artificially Hyperventilated Subjects During Sleep. L. F. Peltier.—p. 614.

Effect of Temperature Change on pH of Human Urine. L. G. Wesson Jr. —p. 619.

Effect of Modified Fluid Gelatin on Renal Function. A. J. Michie, C. E. Koop, W. S. Blakemore and M. C. Ragni.—p. 621.

Effect of Repeated Infusions of Dextran on Renal Function. A. J. Michie and M. C. Ragni.—p. 625.

Relation of Grip Strength and Grip-Strength Endurance of Age. W. E. Burke, W. W. Tuttle, C. W. Thompson and others.—p. 628.

*Specific Dynamic Action of Protein in Men Past 60 Years of Age. W. W. Tuttle, S. M. Horvath, L. F. Presson and K. Daum.—p. 631.

Specific Dynamic Action of Protein in the Aged.—Since widely differing specific dynamic action values in different subjects have been reported, it was thought that the differences might be related to the ages of the subjects. The experiments reported here were done to elucidate any possible role that age may play in the specific dynamic action of protein. The responses of old men (mean age 77 years) and young men (mean age 24 years) to the ingestion of a standard protein test meal, which yielded 25 gm. of protein, were compared. The specific dynamic action, expressed as total excess oxygen utilization, was essentially the same in both age groups. The older subjects exhibited a slower initial response to the protein meal but had both higher peak values and increased excess oxygen utilization during the second half of a 4.5 hours test period.

Journal of Aviation Medicine, St. Paul

24:99-164 (April) 1953. **Partial Index**

Attainment of Specialty Recognition for Aviation Medicine: Role of Interim Board in Petitioning for Certification. R. J. Benford.—p. 101.

Studies of Adrenocortical Function in Long-Distance Fliers: Preliminary Report. J. P. Gofton and S. D. McGrath.—p. 107.

Effect of Moderate Altitude Upon Human Gastric Emptying Time. E. Shocket, M. M. Jackson and H. C. Dyme.—p. 113.

Evaluation of Changes in Eosinophil Levels in Studies of Adrenocortical Function and Stress. J. P. Gofton, B. F. Graham, S. D. McGrath and R. A. Cleghorn.—p. 122.

Study of Eosinophil Response to Exercise in Man. R. F. Wake, B. F. Graham and S. D. McGrath.—p. 127.

Microscopical Observations of Peripheral Circulation at Simulated High Altitudes. B. J. Sullivan and L. D. De Gennaro.—p. 131.

Spectacles in Jet Flying. P. H. Evans and J. W. Peachy.—p. 138.

Clinical Research on Subject of Test on Aviator's Fatigue. R. Monjauze, F. Plas, G. and J. Verdeaux and others.—p. 143.

Journal of Bacteriology, Baltimore

65:355-484 (April) 1953. **Partial Index**

Enzymatic Changes During Sporogenesis in Some Aerobic Bacteria. W. A. Hardwick and J. W. Foster.—p. 355.

Microbacterium Thermosphactum, Spec Nov; Nonheat Resistant Bacterium from Fresh Pork Sausage. R. A. McLean and W. L. Sulzbacher. —p. 428.

Relationships of Viral Content of Living and Dead Whole Eggs Inoculated with Various Concentrations of Psittacosis Virus. M. K. Nadel and O. N. Fellowes.—p. 449.

Role of Bacterial Resistance in Antibiotic Synergism and Antagonism. M. Klein and S. E. Schorr.—p. 454.

Investigations on Biosynthesis of Citrovorum Factor by Lactic Acid Bacteria. D. Hendlin, L. K. Koditschek and M. H. Soars.—p. 466.

Synthesis of Glutamic Acid and Glutamyl Polypeptide by Bacillus Anthracis: III. Factors Affecting Peptide Production in Synthetic Liquid Media. C. B. Thorne, C. G. Gómez, G. R. Blind and R. D. Housewright.—p. 472.

Journal Clin. Endocrin. & Metab., Springfield, Ill.

13:383-488 (April) 1953

Biologic Titration of Diethylstilbestrol Against Activity of Prostatic Cancer: Effect on Serum Aldolase. R. Baker, D. Govan, J. Huffer and J. Cason.—p. 383.

*Does a Large Intake of Potassium Modify Metabolic Effects of ACTH (Corticotropin) in Man? L. L. Bennett, G. W. Liddle and R. C. Bentinck.—p. 392.

Congenital Testicular Deficiency: II. Defective Sertoli Cell Differentiation in Hypogonadism of So-Called "Obscure Origin." A. R. Sohval and L. J. Soffer.—p. 408.

Increased Urinary Estrogen Excretion Associated with Adrenal Tumors: Report of Four Cases. F. C. Dohan, E. Rose, J. W. Eiman and others. —p. 415.

Disappearance of Infused Amino Acids from Plasma of Hospitalized Control and Addisonian Subjects. R. N. Cagan, R. L. Klein and L. Loewe.—p. 429.

Effect of Orally Administered Ascorbic Acid and/or l-Cystine on Urinary Steroid Excretion. J. W. Goldzieher and J. S. Edlin.—p. 436.

Determination of Protein-Bound Iodine by Dry Ashing. H. Brown, A. M. Reingold and M. Samson.—p. 444.

Epilation by Electrocoagulation: Improvements in Technic. M. L. Niedelman.—p. 451.

Changing Concepts in Thyroid Physiology and Therapy. W. O. Thompson.—p. 457.

Modification of the Effects of Corticotropin by Potassium.—It is evident that the potassium-depleting, sodium-retaining, diabetogenic, and catabolic effects of corticotropin are undesirable effects clinically. Studies were undertaken in an effort to determine to what extent the biological activity of corticotropin in man might be modified by the simultaneous administration of large amounts of potassium salts. Five of the seven patients studied had active generalized rheumatoid arthritis, one had disseminated lupus erythematosus, and one had hyperinsulinism. Short-term and long-term studies were carried out. The patients received corticotropin in doses up to 100 units daily and, both separately and in combination, large amounts of potassium salts by mouth (up to 360 mEq. per day of potassium acetate). In most instances six day balance periods were employed. No untoward symptoms occurred, except for occasional nausea. A patient to whom corticotropin had been given for three months and in whom hypokalemia developed did not retain extra potassium when he was given 120 mEq. per day of supplemental potassium while corticotropin therapy was continued. These large doses of potassium salts administered concurrently with corticotropin

did not modify the antirheumatic effects of corticotropin. Other effects of corticotropin that were not prevented included uric acid diuresis, eosinopenia, a rise in urinary nitrogen levels, a rise in fasting blood sugar levels, and a rise in 17-ketosteroid excretion. On the other hand, the effects of corticotropin upon electrolyte metabolism were definitely modified. The sodium retention that occurs when corticotropin therapy is initiated was prevented or diminished by the concurrent administration of adequate amounts of potassium salts. Starting the administration of potassium salts after corticotropin therapy was underway induced prompt diuresis of sodium. The sodium diuresis that ordinarily follows withdrawal of corticotropin therapy may not occur in patients who are receiving potassium salts concurrently. A transient (one to two days) positive phosphorus balance was produced by the administration of large doses of potassium salts.

Journal of Clinical Nutrition, Allentown, Pa.

1:179-266 (March-April) 1953

Lack of Avitaminosis Among Alcoholics: Its Relation to Fortification of Cereal Products and General Nutritional Status of the Population. W. G. Figueroa, F. Sargent, L. Imperiale and others.—p. 179.

Pyridoxine Deficiency in Human Infant. S. E. Snyderman, L. E. Holt Jr., R. Carretero and K. Jacobs.—p. 200.

Arteriovenous Glucose Differences, Metabolic Hypoglycemia and Food Intake in Man. T. B. Van Itallie, R. Beaudoin and J. Mayer.—p. 208.

*Use of Oral High Fat, High Calorie Emulsion for Total Feeding. W. J. Kuhl Jr., M. I. Grossman and C. F. Consolazio.—p. 218.

Effect Upon Serum Cholesterol and Phospholipids of Diets Containing Large Amount of Vegetable Fat. L. W. Kinsell, G. D. Michaels, J. W. Partridge and others.—p. 224.

Oral Administration of High Caloric Fat Emulsion for Total Feeding.—This study was undertaken to ascertain whether a high calorie, high fat liquid feeding could be administered as the sole source of feeding, and if this would be accompanied by gain in weight, restoration of positive nitrogen balance, and minimal alteration in normal metabolism. Six patients with fracture of the mandible and wiring received a high calorie liquid feeding, consisting primarily of a 40% emulsion of peanut oil, to which was added a protein concentrate and vitamins and minerals. In the preparation 100 gm. of protein concentrate, which also contained vitamins and minerals, was added to 1,000 ml. of the fat emulsion; 100 mg. of ascorbic acid, 4.0 gm. of sodium chloride as an isotonic solution, and 85 mg. of iron as ferric ammonium citrate were added. The preparation was mixed in a blender and refrigerated until consumed. Five of the patients consumed the arbitrarily determined amount of 1,000 ml. of the fat emulsion and supplements daily in divided feedings, which provided 4,370 calories. The sixth patient varied his daily intake over the period of study, beginning with a smaller amount of the preparation. The five patients gained weight while receiving the fixed amount of 1,000 ml. of fat emulsion. The weight gain ranged from 2.75 to 12.25 lb. (1,247 to 5,528 gm.) in from 12 to 24 days. The average daily weight gain was 0.4 pounds (181 gm.). Fecal fat excretion increased 7.68 gm. above the control level. No consistent changes occurred in fasting blood levels of total or neutral fat, phospholipid, cholesterol, serum total protein or albumin/globulin ratio, nonprotein nitrogen, fasting blood sugar, or carbon dioxide content.

Journal of Experimental Medicine, New York

97:467-589 (April) 1953. **Partial Index**

In Vitro Production of New Types of Hemophilus Influenzae. G. Leidy, E. Hahn and H. E. Alexander.—p. 467.

Osmotic Homeostasis Maintained by Mammalian Liver, Kidney, and Other Tissues. E. L. Opie and M. B. Rothbard.—p. 483.

Effect of Temperature on Growth of Virus-Induced Frog Carcinoma: II. Temperature Coefficient of Growth in Vitro. B. Lucké, L. Berwick and P. Nowell.—p. 505.

Observations Concerning Production and Excretion of Cholesterol in Mammals. IX. Mechanism of Hypercholesteremic Effect of Cholic Acid. S. O. Byers, M. Friedman, M. W. Biggs and B. Gunning.—p. 511.

Induced Malignancy in Cells from Rat Myocardium Subjected to Intermittent Anaerobiosis During Long Propagation in Vitro. H. Goldblatt and G. Cameron.—p. 525.

Journal of Immunology, Baltimore

70:331-434 (April) 1953

Specific White Cell Lysis Produced by Combination of Rabbitt Antiserum to Purified Protein (Ovalbumin, Bovine Gamma Globulin) with Homologous Antigen. Role of Non-Precipitating Antibody. B. H. Waksman.—p. 331.

Comparative Retention of Antigen in Skin of Immune and Normal Rabbits as Determined with Egg Albumin Labelled with Radioactive Iodine. L. Korngold, G. L. Stahly, M. C. Dodd and W. G. Myers.—p. 345.

Stability of Chick Embryo Yellow Fever Vaccine During Storage. R. G. Hahn and J. C. Bugher.—p. 352.

Origin of Fecal Antibody and its Relationship to Immunization with Adjuvant. M. E. Koshland.—p. 359.

Effect of High Intensity Electron Bursts on Antibodies. F. R. Traub, A. Brasch and W. Huber.—p. 366.

Molecular Weight of Antigen-Antibody Complex. E. L. Becker.—p. 372.

Effects of Spleen Shielding and Subsequent Splenectomy Upon Antibody Formation in Rats Receiving Total-Body X-Irradiation. R. W. Wissler, M. J. Robson, F. Fitch and others.—p. 379.

Some Effects of Formalin on Serological Activity of Crustacean and Mammalian Sera. C. A. Leone.—p. 386.

Antigenic Variation of Influenza B Viruses, Demonstration of Antigenic Spectrum by Use of Titer Ratios. W. S. Jordan Jr. and S. G. Gaylin. —p. 393.

Characteristics of Antibiotic-Producing Strains of Ocular Bacterial Flora. S. P. Halbert, L. Swick and C. Sonn.—p. 400.

Altered Reactivity of Mice After Immunization with Hemophilus Pertussis Vaccine. L. S. Kind.—p. 411.

Relation of Incubation Period and Secondary Immune Response to Lasting Immunity to Infectious Diseases. C. M. MacLeod.—p. 421.

Bio-Assay of Four Tetanus Toxoids (Aluminum Precipitated) in Mice, Guinea Pigs and Humans. J. Ipsen Jr.—p. 426.

Journal Lab. and Clinical Medicine, St. Louis

41:499-662 (April) 1953. **Partial Index**

Biological Studies with Arsenic^{76}: IV. Histopathologic Effect of Arsenic^{76} Upon Hematopoietic Tissues of Patients with Leukemia. M. Block, L. O. Jacobson and W. Neal.—p. 499.

Rate of Formation of Nondiffusible (Organic) Fraction of I^{131} in Plasma Correlated with Apparent Thyroid State. W. E. White.—p. 516.

Radioactive Iodine-Labeled Fat. M. C. Hoffman.—p. 521.

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Effect of Bacterial Pyrogen Upon Experimental Cardiovascular and Renal Lesions of Anaphylactic Hypersensitivity. I. L. Bennett Jr., L. B. Guze and E. Roberts.—p. 559.

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*Nitrogen Metabolism and Liver Histology During Aureomycin Administration in Patients with Hepatic Disease. W. W. Faloon, J. W. Noll and J. T. Prior.—p. 596.

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Bilirubin and Protein in Cerebrospinal Fluid of Jaundiced Patients with Severe Liver Disease With and Without Hepatic Coma. D. S. Amatuzio, L. J. Weber and S. Nesbitt.—p. 615.

Influence of Antihistaminic Agents on Erythrocyte Agglutination.—Reduction in the incidence of unfavorable transfusion reactions, which is important to leukemic patients and others requiring frequent and multiple transfusions, may be secured by adding certain antihistaminic agents to whole blood before its infusion. A significant retardation of the specific agglutination in vitro of group A and group B erythrocytes was noted when diphenhydramine (Benadryl) was added to anti-A and anti-B serums, and this led to further study of the inhibiting effect of diphenhydramine and other antihistaminic agents on isoagglutination of human blood cells in vitro. Tests of eight agents showed that diphenhydramine and pyrilamine malęate apparently had the greatest inhibitory effect on isoagglutination.

Methapyrilene (Histadyl) and tripelennamine (Pyribenzamine) exerted a slight inhibitory action, and cyclopentamine (Clopane) hydrochloride, antazoline (Antistine), a mixture of phenylephrine (Neo-Synephrine) and Thenfadil (*N*-[2-dimethylaminoethyl]-*N*-2-pyridyl-3-thenylamine), and dimenhydrinate (Dramamine) had essentially no effect. The use of diphenhydramine and tripelennamine in vivo appears to protect the recipient more effectively than can be accounted for by the results obtained in vitro. The isoagglutination reaction is retarded and weakened when antihistaminic agents are used in vitro, but eventual clumping of the cells is not prevented; in vivo, however, the retardation is apparently sufficient to overcome minor clumping due to atypical antibodies, thus preventing the characteristic clinical responses that usually follow. Sensitized erythrocytes from an infant with erythroblastosis fetalis were used to test the effect of antihistaminic agents on the anti-human-globulin (Coombs') reaction. Agglutination appeared to be retarded by pyrilamine maleate, tripelennamine, and dimenhydrinate. Only slight retardation was observed with cyclopentamine hydrochloride and the mixture of phenylephrine and Thenfadil, and the effect of the other agents, methapyriline, antazoline, and diphenhydramine, could not be evaluated because they produced hemolysis of the sensitized erythrocytes.

Nitrogen Metabolism and Liver Histology During Aureomycin Treatment.—Three patients with alcoholic fatty cirrhosis and one with convalescent hepatitis receiving aureomycin therapy were studied in an effort to determine the effect of aureomycin on nitrogen metabolism, liver histology, and liver function tests. Urine nitrogen excretion was increased in all four patients while they were receiving aureomycin, and the nitrogen balance became negative in two, although their diet remained constant. Methionine deficiency has been suggested as the cause of aureomycin-induced nitrogen loss, but simultaneous administration of methionine had no effect on nitrogen excretion in these patients. Fatty infiltration of the liver was observed after two weeks of aureomycin therapy in one patient and was not reversed when methionine was administered concurrently for another two weeks. Biopsy of the liver 10 days after administration of aureomycin was stopped showed almost complete disappearance of the fatty changes. Liver histology was improved or unchanged in the other three patients, in whom aureomycin therapy was limited to brief periods (five to seven days). Individual variations in the susceptibility of patients to fatty infiltration may account for the varying findings reported in this and other studies. No serious hepatic deterioration under aureomycin therapy was shown by any of the functional tests employed, but its prolonged use in conditions in which protein anabolism is therapeutically desirable would probably be injudicious.

Journal Pharmacology & Exper. Therap., Baltimore

107:403-536 (April) 1953

Pharmacology of N-Benzyl-β-Chloropropionamide (Hibicon), A New Anticonvulsant. B. K. Harned, R. W. Cunningham, M. C. Clark and others.—p. 403.

Nicotinolytic Drugs: II. Action of Adrenergic Blocking Agents on Nicotine-Induced Tremors. R. L. Cahen, J. M. Thomas and K. M. Tvede. 4—p. 424.

Effects of Thiopental and Pentobarbital on Voluntary Muscle. C. P. Kraatz, M. I. Gluckman and H. L. Shields.—p. 437.

Pharmacology of Vinyl Ethynyl Carbinols—New Class of Central Nervous System Depressants. S. Y. P'An, J. F. Gardocki, M. Harfenist and A. Bavley.—p. 459.

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Journal of Thoracic Surgery, St. Louis

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*Results of Thoracoplasty for Pulmonary Tuberculosis 11 to 16 Years After Operation: Complete Follow-Up Report. A. H. Aufses and M. S. Harte.—p. 329.

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Volvulus of Lobe of Lung as Complication of Diaphragmatic Hernia: Case Report. H. T. Ransdell Jr. and R. G. Ellison.—p. 341.

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*Repair by Full Thickness Skin Graft of Penetrating Wounds of Intrathoracic Trachea: Report of Case. J. M. Hanner and S. H. Cohen. —p. 380.

*Tracheal Resection and Replacement with Prosthesis. R. L. Craig, G. W. Holmes and E. J. Shabart.—p. 384.

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Pancoast Syndrome Due to Bronchiogenic Carcinoma: Successful Surgical Removal and Postoperative Irradiation: Case Report. W. M. Chardack and J. D. MacCallum.—p. 402.

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Neurofibromatosis with Intrathoracic Neurofibromas of Vagus Nerve: Report of a Case Associated with Pectus Excavatum. F. Gerbode and G. S. Marguiles.—p. 429.

Late Results of Thoracoplasty for Pulmonary Tuberculosis.—Thoracoplasty was done for pulmonary tuberculosis in 90 patients between 1935 and 1940 who were followed for 11 to 16 years. Six died postoperatively and four within the first year after the intervention. In the 80 patients living in 1941, the disease had been arrested in 64 and not arrested in 16. In 57 of the 64 patients the disease has remained inactive up to the present time. One patient with negative sputum committed suicide two years after the operation. Two patients who had inactive disease for long periods died of nontuberculous causes. Four patients had reactivation of their tuberculosis, but the disease has again become inactive in one. Of the 16 patients who still had positive sputums at the time of the first report, 6 had late sputum conversion, and subsequently the disease has remained inactive. One patient is clinically well, with occasional positive cultures, and is classified as having arrested disease. Active tuberculosis persisted in nine patients; eight of these died from 4 to 10 years after the operation and one is still alive. Thus 66 of the 80 patients alive in 1941 are still alive, 63 with inactive disease, one with arrested disease, and two with active tuberculosis. Four of the 14 who died had inactive disease at the time of death. Today, with the addition of the antibiotics, thoracoplasty performed on a selected group of patients should yield a very high percentage of early good results that can be expected to be maintained over a long period.

Repair of Wounds of Intrathoracic Trachea.—A 20-year-old private in the marine corps of the republic of Korea was struck by a bullet that entered his body in the left supraclavicular region and emerged through the right eighth intercostal space posteriorly. The patient had a right tension pneumothorax with pronounced mediastinal shift to the left. Endotracheal intubation was carried out and a posterolateral thoracotomy was performed through the eighth interspace. The left lung was almost completely collapsed, and it was soon apparent that a large defect was present in the trachea just proximal to the coryna. On careful dissection of this area two perforations were noted: an anterior longitudinal defect 2 cm. in length just proximal to the coryna, and another of the same size and type, just proximal to the anterior defect, on the esophageal aspect of the trachea. Despite these defects sufficient pulmonary aeration had prevailed to sustain life 24 hours. The vagus nerve was carefully dissected away, and the anterior tracheal defect was closed with interrupted silk sutures. The

posterior defect was difficult to approach for suturing. A full thickness skin graft, large enough to encircle the posterior defect as well as to allow for retraction, was obtained from the patient's anterior abdominal wall. The graft was everted and passed around the trachea with the skin surface applied to the tracheal defect and the subcutaneous tissue in contact with the esophagus and other mediastinal structures. The graft was then sutured anteriorly with interrupted silk sutures to form a cuff around the tracheal defect, then sutured to the trachea superiorly and inferiorly on the anterior surface. Following this procedure, the lung could be expanded with positive pressure and without evidence of seepage of air or fluid through the defects or around the skin graft. A large catheter was inserted through a stab wound in the ninth interspace. The incision was then closed in layers. Bronchoscopy was performed following the operative procedure. The trachea was patent and dry. The thoracotomy tube was removed on the fourth postoperative day. Closure of the donor area on the anterior abdominal wall was performed on the 26th postoperative day by mobilization of superior and inferior skin flaps. A tracheogram performed on the 28th postoperative day showed an adequate tracheal lumen with a small area of indentation where the skin graft had been applied. The patient is well two months following operation.

Tracheal Resection and Replacement with Prosthesis.—Experiments to determine whether or not it would be possible to make a complete segmental resection of a portion of the trachea and replace this segment with a prosthesis were carried out on dogs. Results showed that the trachea can be resected in the neck or thorax of the animals and that the trachea will regain its continuity over a prosthesis. The prosthetic tube used was constructed of layers of fused polyethylene in which wire was incorporated to prevent cutting through of the sutures with motion. This permitted adequate fixation until continuity was reestablished, and in some instances the anastomosis could be instituted and maintained as an airtight channel. While a segmental tissue defect will regenerate with fibrous tissue, however, this tissue is not capable of supporting itself and stenosis will result when the prosthesis is removed. True tracheal regeneration did not occur. This would indicate that a prosthesis to replace the entire circumference of a resected segment will not be practical to use on human patients. In addition, a prosthesis offers a mechanical barrier to the evacuation of bronchial secretions. Because the prosthesis can be sutured without the sutures cutting out, this type of prosthesis might find other use as replacement for damaged or destroyed blood vessels or possibly resected esophageal segments. In a 63-year-old patient with squamous cell carcinoma of the trachea, the anterior half of the trachea containing the tumor was resected and a polyethylene tube prosthesis was placed to occupy the defect. The incision was closed after fixation of the prosthesis in place with interrupted sutures around the perimeter of the tracheal defect. On the second postoperative day partial atelectasis of the right lung developed that resulted in death the next day. Necropsy revealed an enlarged right heart, mediastinitis, and partial atelectasis of the right lung.

Medical Annals of District of Columbia, Washington

22:169-220 (April) 1953

*Subdural Effusions in Infancy. H. Stevens and J. M. Williams.—p. 169.
Effects of Oral Administration of Pentylenetetrazol and Barbiturate Combinations. T. Koppanyi and J. F. Fazekas.—p. 175.
Hypokaliemia in Porphyria. C. W. Thompson and A. E. Parrish.—p. 177.
Dermatitis from Fabrics. L. Schwartz.—p. 179.
Relationship of Gastric Ulcer to Gastric Cancer. G. T. Pack, A. O. Hampton, F. C. Helwig and others.—p. 185.

Subdural Effusions in Infancy.—Clinicians are now compelled to give their attention to new complications and new sequelae of previously lethal diseases. Subdural effusion in childhood is one of these. This condition usually begins with meningitis in an infant aged 1 year or less. With appropriate antibiotic therapy a "cure" is effected, but the infant remains or becomes listless, pale, anorexic, and irritable. The meningitic process is often blamed, and the conclusion is drawn that irreparable brain damage has resulted from the acute illness and accounts for the whole process. Convulsions, focal paralysis, and stupor may also occur. Stevens and Williams feel that their observations on 30 cases of nontraumatic subdural effusion suggest that this is a common lesion, which can be diagnosed, and that corrective measures may be necessary to prevent neurological complications and to salvage the child's mentality. If the diagnosis is suspected, bilateral subdural taps should be made at the extreme lateral margin of the anterior fontanel or through the coronal suture about midway between the extreme corner of the fontanel and the zygoma. If more than 2 cc. of fluid is found, subdural effusion may be said to be present. The volume obtained with each subdural drainage varies, and in some cases the subdural space eventually "dries up." Whether the subdural effusion can be completely eliminated and all symptoms resolved without sequelae by repeated subdural taps can be determined only by further studies. It is the impression of these authors that, even if the effusion is "dried up" by repeated drainage, a vascularized thickened neomembrane may still remain to encapsulate the brain and strangle its growth. The authors present case histories. These subdural effusions usually occur in infants less than 1½ years old following meningitis, which is usually due to Hemophilus influenzae or Diplococcus pneumoniae. No single diagnostic criterion is reliable, but the history of any meningitis should arouse suspicion, particularly if the child's physical and mental development is not progressing. Subdural taps are essential in such a condition and are considered safe and simple. If subdural fluid persists, it may be inferred that a constricting membrane has formed, necessitating surgical removal in most instances. Morbidity from this membrane may be grave. In addition to meningitis as a cause of subdural effusion, the clinician should be alert to the possibility of such effusion occurring in cachectic children, for example, in children with chronic severe diarrhea. The treatment is the same.

Michigan State Medical Society Journal, Lansing

52:345-464 (April) 1953

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Opinion Evidence from Medical Experts. B. Doelle.—p. 394.
Malpractice as Seen by a Lawyer. C. C. Purdy.—p. 402.
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Minnesota Medicine, St. Paul

36:289-432 (April) 1953

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Hundred Years of Progress in Therapy of Urinary Infection. W. F. Braasch.—p. 378.
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Neurology, Minneapolis

3:77-162 (Feb.) 1953

Occlusion of Superior Cerebellar Artery. J. A. Luhan and S. L. Pollack. —p. 77.
Studies on Cervical Spinal Cord of Man: Sensory Pattern After Interruption of Posterior Columns. B. Boshes and F. Padberg.—p. 90.
Background Illumination and Visual Threshold in Hemianopic Areas. M. B. Bender and H. P. Krieger.—p. 102.
*Bodily State in Injuries of Spinal Cord. H. Chor, I. Finkelman and H. Blustein.—p. 111.
Disorders of Electrolyte Metabolism in Diseases of Central Nervous System. I. S. Cooper.—p. 119.
Neurologic Complications of Hemorrhagic Diseases. W. S. Chalgren. —p. 126.
Spinal Fluid Findings Following Cerebral Angiography. J. M. Stein and M. Fink.—p. 137.

Bodily State in Injuries of Spinal Cord.—The nervous regulation of various bodily functions requires that the influences from centers in the cerebral cortex, diencephalon, and brain stem be transmitted through the autonomic nervous system. Many of these influences reach the viscera or tissues to be regulated through the spinal cord. In injuries of the spinal cord, most attention has been given to the disturbances in motion, sensation, reflexes, bowel and bladder function and the nutritional state, particularly bed sores. Alterations in other bodily functions, such as cardiovascular regulation, glucose metabolism, water metabolism, temperature regulation, and gastrointestinal activity, have been given little attention. Chor and his associates found the basal blood pressure to be low in cervical cord lesions. Orthostatic hypotension occurred oftenest in cervical cord lesions, and momentary loss of consciousness often resulted when the erect position was attempted. A reverse reflex hypertension, with headache and other unpleasant sensations, occurred during the administration of enemas. Glucose tolerance curves were abnormal, although there was no evidence of disease of the liver, pancreas, adrenal glands, and thyroid. There was a defect in concentration of the urine as well as in the day-night ratio, in the absence of signs of kidney disease. There was stasis in the colon as determined by charcoal excretion tests. Gallbladder evacuation and concentration were normal. Diarrhea was observed occasionally. A constant finding in cord injuries was a great loss of weight, which usually was not regained. Hunger and thirst were experienced as well as a sensation of fullness after eating. Nausea was produced by various stimuli as well as by retained feces and calculi. Hiccoughs were due to the usual causes. The water intake was greatly increased, particularly in cervical cord lesions. Death in patients with spinal cord lesions has usually been attributed to infection, especially of the urinary tract and terminally of the lungs. In analyzing the clinical histories of those who died the authors found that in most cases genitourinary infections were not the only cause. Many of them had had recurrent attacks of sepsis. Most of them had had several surgical procedures performed. Severe decubitus, osteomyelitis, heart lesions, pulmonary disease, gastrointestinal complications, and general nutritional disturbances were encountered. Even when the terminal picture was that of uremia due to kidney failure, other factors contributed to the fatal outcome in many cases.

New England Journal of Medicine, Boston

248:621-664 (April 9) 1953

*Betaine and Glycocyamine in Treatment of Poliomyelitis. A. L. Watkins. —p. 621.
Interpretation of One-Stage Method for Determining Prothrombin Time. A. J. Quick and C. V. Hussey.—p. 624.
Renal Thrombosis Complicating Epidemic Diarrhea of Newborn: Nephrectomy with Recovery. H. W. Clatworthy Jr., D. R. Dickens and C. R. McClave.—p. 628.
*Plantar Warts: Cure by Injection. E. C. Branson and R. L. Rhea Jr. —p. 631.
Pharmacologic Aspects of Adrenocortical Steroids and ACTH in Man (Concluded). G. W. Thorn, D. Jenkins, J. C. Laidlaw and others. —p. 632.

Betaine and Guanidineacetic Acid in Treatment of Poliomyelitis.—The purported value of betaine and guanidineacetic acid (glycocyamine) was investigated in nine patients who had residual muscle weakness following an attack of poliomyelitis one or more years previously. All of them were cooperative adults who had reached a stage at which increases in muscle function were absent or minimal. A 10th patient was studied who had had infectious polyneuritis several years previously, with residual paralysis of the muscles of both legs. To make the evaluation as objective as possible, the strength of the muscles studied was measured by means of a special instrument known as a Myodynemeter, utilizing a strain gage with a calibrated recording device and standardized test positions. A total of 76 muscle actions were recorded, since 2 to 13 different muscles were tested in each of the 10 patients. Tests of the following muscle actions were included: wrist flexion and extension; elbow flexion and extension; shoulder internal rotation, vertical and horizontal abduction, and extension and flexion; foot dorsiflexion, eversion, inversion and combined dorsiflexion and inversion, and knee extension and flexion; and hip flexion, extension, adduction, abduction, internal rotation, and external rotation. The patients were given guanidineacetic acid in daily doses of from 3 to 5.5 gm. and betaine in doses of 20 or 25 gm. daily. The patients were told that this was an experimental study to determine the benefits of new drugs. Efforts were made not to show any enthusiasm for the drugs. Only 26% of the muscles tested showed as much as a 20% increase in strength, which did not appear significant subjectively or functionally. When increases in strength occurred, they appeared in muscles that had not received intensive exercise to increase power. Under the conditions of this study, betaine and guanidineacetic acid were not considered to have significant value in the treatment of muscle weakness resulting from poliomyelitis.

Plantar Warts: Cure by Injection.—The simple treatment here described was accidentally discovered by a surgical technician, who, having been approached by a soldier with a plantar wart and a desire to march in a special parade, injected the wart with procaine (Novocain) as a temporary expedient. The soldier marched in the parade, and in a few days the plantar wart disappeared. After this the method was successfully applied in 48 patients. It has been possible to follow 30 of these for six months and 22 of them were cured. In seven cases a plantar wart was still present but was asymptomatic. Only one patient showed no improvement after three injections. Three patients in the series had extensive plantar warts of the mosaic type and were cured. One of these had approximately 30 warts involving the entire plantar surface of the left foot, and treatment by any of the currently accepted methods would have been extremely difficult. The treatment consists of the injection of 2 or 3 cc. of 1% procaine under pressure into the base of the wart in the stratum germinativum layer of the epidermis. Best results are obtained with the use of a 26-gage needle and a Luer-Lok dental syringe. The needle should penetrate to the stratum germinativum through normal skin at the side of the wart; and only one needle puncture should be made, because the injected fluid escapes through multiple holes and sufficient pressure cannot be obtained. If the needle is properly placed, there is considerable resistance to injection, and the desired marked blanching of the skin and elevation of the wart will result. Patients usually become symptom-free within 24 hours. In five to seven days the wart becomes soft and darkened. Usually, it can be lifted out with a thumb forceps after a week.

248:665-708 (April 16) 1953

Whipple's Disease: Report of Case with Special Reference to Histochemical Studies of Biopsy Material and Therapeutic Results of Corticosteroid Therapy. C. M. Jones, J. A. Benson Jr. and A. L. Roque. —p. 665.
*Pseudoprecocious Puberty in Girls as Result of Estrogen Ingestion. C. D. Cook, J. W. McArthur and W. Berenberg.—p. 671.
*Problems and Practices in Community Hospital: II. Postoperative Stricture of Biliary Tract. F. R. Pierce and J. P. Marnane.—p. 674.
Role of Cortisone in Treatment of Severe Bronchial Asthma. W. S. Burrage and J. W. Irwin.—p. 679.
Urology. F. H. Colby.—p. 682.
*Vitamin A Intoxication: Report of Case in an Adult. E. Bifulco. —p. 690.
Practical Use of Cooling Device to Inhibit Cutaneous Pain of Hypodermic Injections. H. L. Mueller.—p. 692.

Pseudoprecocious Puberty as Result of Estrogen Ingestion.—The first of the two patients with pseudoprecocious puberty who are described here was a girl, 4 years and 3 months old. She was referred to the hospital because of tenderness

and enlargement of both breasts, with dark pigmentation of the areolae, of three weeks' duration. Two days before admission scanty vaginal bleeding had occurred. A preoperative diagnosis of a solid tumor of the left ovary (with a question of granulosa cell tumor) was made, and an exploratory laparotomy performed. The uterus and fallopian tubes proved to be enlarged and hyperemic, but no abnormal masses were found. Histological studies of biopsy material showed normal preadolescent ovarian tissue, with no evidence of follicular activity. After the laparotomy further questioning revealed that diethylstilbestrol had been in the house and easily available to the child, the mother having taken the drug until four months before the appearance of the child's precocious breast development. Follow-up examination one month postoperatively showed complete regression of the breast enlargement and a considerable decrease in the pigmentation. No further vaginal bleeding had occurred. The second case occurred in a 7-year-old girl, who was referred to a Children's Medical Center because of bilateral breast enlargement of four weeks' duration and vaginal bleeding that had begun three days before admission. Further investigation revealed that the child, who attended a boarding school, was taking four pills three times a day that supposedly were vitamin preparations. Bioassay of the suspicious tablets in female rats revealed the presence of estrogenic activity. Further inquiry established the fact that the patient's father had mistakenly given her diethylstilbestrol instead of ascorbic acid tablets. Examination two months later showed that the signs of precocious puberty had disappeared. The authors suggest that areolar pigmentation in young girls might suggest the possibility of diethylstilbestrol ingestion. They advocate postponing laparotomy for two to four weeks when the pelvic findings are negative or equivocal.

Postoperative Stricture of Biliary Tract.—Pierce and Marnane describe four cases of loss of continuity of the common bile duct after cholecystectomy, at least three of which are attributable to surgical bile duct injury. In the fourth case an inflammatory process seemed largely responsible. A surgeon's prompt realization in one of the cases of the probable cause of the difficulty, which developed a few days after a presumably uncomplicated operation, and his immediate referral of the case to a surgeon with greater experience in the treatment of such injuries proved to be very important. It is now six years since the last common duct injury occurred in the hospital with which the authors are connected. At that time the surgical staff discussed gallbladder disease and stressed that even in the "easy" cases caution is required. There is a high incidence of congenital anomalies of the biliary system. The surgeon should familiarize himself early in the operation with the exact location of the structures of the gastrohepatic ligament, so that bleeding from the cystic artery may be controlled by pressure of the hepatic artery between the thumb and forefinger, obviating the hasty, blind application of clamps. The angle between the cystic duct and the common duct should be well exposed. The cystic artery should be exposed to its entrance to the gallbladder and tied close to this point. It is safer to tie the cystic duct before clamping, and the clamp should be distal to the well-visualized tie. One should beware of applying ties or clamps while traction is applied to the gallbladder. The duct system with lax peritoneal investments is easily knuckled. In acute cases, if the landmarks are obliterated by edema, a cholecystostomy may be the operation of choice. Secondary removal of the gallbladder is a far less formidable procedure than repair of the injured ductal system. At the end of a cholecystectomy, the bile ducts should be carefully inspected; if the surgeon finds that injury has occurred, he should repair it immediately. Any surgeon who undertakes a gallbladder operation should be ready to carry out this procedure. If it becomes apparent early in the postoperative period that injury has occurred, a surgeon experienced in plastic repair on the biliary tract should be consulted at once, so that repair will not be further complicated by increased scar tissue of unsuccessful secondary operations.

Vitamin A Intoxication in an Adult.—A 52-year-old woman was seen in consultation by the author because her physician wanted to ascertain the cause of spontaneous bleeding from the mucous membranes. She had had generalized flaking of the skin since childhood, and about 4½ years previously cracking and oozing about the skin of the legs had developed. When various treatments did not give relief, her physician started vitamin A therapy. In the early part of 1948 she received 150,000 I. U. of vitamin A and 100 mg. of an antihistamine daily for the first week and 100,000 units of vitamin A daily thereafter. The latter dose of vitamin A was taken from the early part of 1948 until Feb. 29, 1952. Insomnia and listlessness began in the early part of 1949. Another year elapsed before she began to note loss of scalp hair. Extraction of the upper teeth exemplified the danger of hemorrhage from the gums and mucous membranes and its correction by administration of vitamin K. The relation of pulsating exophthalmos to vitamin A intoxication, if any, is unknown. The patient never complained of a pulsating headache until a month before vitamin A therapy was stopped; the headaches still persist. The fact that she was completely relieved of her joint pains and aching bones, with regrowth of lost hair within six months of discontinuation of ingestion of vitamin A, is interpreted as evidence of toxicity to vitamin A ingested in large doses over a prolonged period. This case proves that vitamin A intoxication is not limited to infants and children. Sulzberger and Lazar recently described this syndrome in an adult who was inspired to self medication with large doses of vitamin A by a radio "nutrition commentator." In its major clinical manifestations the syndrome appears to be the same whether it occurs in children or adults. This case again emphasizes and confirms the opinion of previous authors that "physicians administering large doses of vitamin A must be on the lookout for signs and symptoms of toxicity."

New York State Journal of Medicine

53:593-720 (March 15) 1953

Carcinoma of the Lung. H. C. Maier.—p. 650.
Clinical Effect of ACTH on Acute Rheumatic Fever. J. T. Aquilina and C. E. Bathrick.—p. 655.
Female Senility: Report of Series of 217 Cases Using Glutest, New Fortified Androgen. W. L. Gould and I. Strosberg.—p. 661.
The Haematype System: Method for Recording Blood Grouping and Rh_0 Determination Permanently, Accurately, and Rapidly: Preliminary Report on Evaluation Study. M. Schlachman and A. Saccone.—p. 667.
Admission to Hospital: Stumbling Block in Impending Delirium. M. Levin.—p. 669.
*Evaluation of Pancreatic Function Tests. D. A. Dreiling Sr.—p. 671.
Clinical Evaluation of Phenylbutazone (Butazolidin), New Antiarthritic Agent. C. S. Byron and H. B. Orenstein.—p. 676.
Electrocardiographic "Abnormalities" in Noncardiac Patients: Clinical Studies of Effect of Some Dihydrogenated Ergot Alkaloids on Certain Electrocardiographic Abnormalities. M. I. Salomon.—p. 681.
Treatment of Headaches. M. M. Braaf and S. Rosner.—p. 687.
Removable Foam Rubber Forceps Mittens. E. M. Greenberg.—p. 694.

Pancreatic Function Tests.—In reviewing the more important laboratory method of studying external pancreatic function Dreiling considered (1) the examination of blood enzymes, (2) examination of feces, and (3) examination of duodenal drainage. The results of studies on patients with normal and abnormal pancreatic function are presented in tables, and the author arrives at the following conclusions: 1. Blood amylase elevations, when present, are of diagnostic significance, but no correlations can be made on a quantitative basis. The results of the various so-called provocative blood enzyme tests are indeterminate. 2. Chemical analysis of the stool furnishes information as to the completeness of digestion and absorption but cannot be used as a reliable quantitative index of pancreatic function. The secretin test yields quantitative data concerning the external pancreatic secretion. Its value in the diagnosis of acute pancreatitis is limited by the rapidity with which the external secretion returns to normal ranges. Pancreatic cancers and chronic pancreatitis can be diagnosed by the characteristic alterations produced in the secretin test responses. In the advanced stages of both diseases, the secretin responses are no longer diagnostically distinct. To overcome this drawback, some investigators combined the secretin stimulus with insulin, methacholine (Mecholyl), or bethanechol (Urecholine). These agents, although potent enzyme stimuli, have the disadvantage of producing not only cardiovascular side-reactions and disturbing changes in gastrointestinal motility but also of stimulating the production of large amounts of gastric acid. The author feels that a standardized preparation of a pancreatic enzyme is needed to complete the secretin test.

North Carolina Medical Journal, Winston-Salem

14:137-176 (April) 1953

Drug Therapy in Tuberculosis. J. S. Hiatt Jr.—p. 137.
Pharmacologic Approach to Obstetric Anesthesia and Analgesia. C. E. Flowers Jr.—p. 140.
Pyogenic Abscess of Liver. E. R. Raylor and H. M. Schiebel.—p. 144.
Massive Tumor of Parotid Gland; with Report of Case. J. F. Patterson Jr.—p. 150.
Abnormal Conditions Resulting from Uncontrolled Emotions. O. R. Yost. —p. 156.
Retrolental Fibroplasia in Piedmont North Carolina. T. D. Ghent and R. W. Roberts.—p. 159.

Northwest Medicine, Seattle

52:267-346 (April) 1953

Selective Radicalism in Treatment of Carcinoma of Stomach. R. S. Smith.—p. 286.
Surital Sodium for Complementation of Spinal Anesthesia. A. C. Kirchhof and D. F. Newcomb.—p. 289.
Vitamin B_{12} in Massive Dosages for Herpetic Lesions: Preliminary Report. G. B. Leitch.—p. 291.
*Toxaphene Poisoning—Report of Fatal Case. R. W. Pollock.—p. 293.
Changing Panorama of Medical Care and Some of Its Implications in Medical Education. E. L. Turner.—p. 295.

Fatal Case of Toxaphene Poisoning.—Toxaphene is widely used as a pesticide against agricultural insects. It is used as a dust, emulsion, spray, wettable powder, and bait. When ingested, toxaphene acts on the central nervous system and causes generalized convulsions of a tetanoid or clonic nature. The selective activity of toxaphene on the central nervous system is best explained by its high lipoidal solubility. All species of animals used in testing this pesticide manifested generalized convulsions. Sublethal doses caused shorter and fewer convulsions. If the dose was lethal, death was due to respiratory failure after a series of convulsions of increasing severity. Warning symptoms such as nausea, abdominal cramps, and vomiting are absent in toxaphene poisoning. Convulsion with loss of consciousness is the cardinal symptom. In the treatment gastric lavage with strong saline solution is used to clean the stomach and saline cathartics to clean the intestines. Dogs survive ingestion of large doses of toxaphene when it is administered in an indigestible oil. Mineral oil, when given early, is effective in decreasing absorption and therefore should be given by prompt gavage or by mouth. The drugs of choice in combating the convulsions in experimental animals are the barbiturates. The authors report a fatal case in a girl, aged 16 months, who was found playing in the yard with a thick, molasses-like substance on her face and hands, the source being a discarded gallon can. After reading the directions on the label, the mother washed the child's face and hands and gave one-third of a glass of salty water. Fifteen minutes later the child was forced to drink one-half of a glass of salty water. The child did not vomit. One-half hour later the mother noticed that the child was limp and turning blue. The child was at once driven to the hospital, but convulsions started en route and never ceased until 10 minutes before death, three and one-half hours later.

Obstetrical & Gynecological Survey, Baltimore

8:155-310 (April) 1953. **Partial Index**

*Spontaneous Rupture of Apparently Normal Uterus During Pregnancy: Review. L. B. Felmus, P. Pedowitz and S. Nassberg.—p. 155.
Possible Role of Smegma in Etiology of Squamous Cell Carcinoma of Cervix Uteri (With Short Review of Literature). R. Fischer.—p. 232.

Spontaneous Rupture of Uterus During Pregnancy.—This review is concerned only with spontaneous rupture of the uterus during pregnancy without apparent cause. In addition to 116 cases found in a thorough search of the literature, 5 new cases are described, 3 observed by the authors of this paper and 2 from other hospitals. Although there may be no apparent cause for rupture of the gravid uterus, careful analysis of the patient's history may reveal a predisposing factor. Except for previous cesarean section and myomectomy, the most common predisposing factors for rupture of the uterus before the onset of labor are previous intra-uterine manipulation (such as curettage and manual removal of the placenta) and postabortive or postpartum sepsis. Intra-uterine infection during pregnancy also may be a cause of rupture. Thrombosis of a uterine blood vessel with infarction of the myometrium is reported for the first time as a cause for rupture before labor. Among the less common causes are adenomyosis uteri with excessive trophoblastic penetration of the myometrium, the thinned uterine wall of the multipara, congenital abnormalities of the uterus, and cornual or angular pregnancies. Spontaneous rupture of the uterus during pregnancy is most frequent during the last trimester but may occur as early as the fourth month. Rupture before the sixth month of gestation occurred in 35 cases and after the sixth month in 71 cases. The time of rupture in the remaining 15 cases was not recorded. In contrast to the characteristically lower uterine segment rupture during labor, the laceration during pregnancy is almost always in the corpus of the uterus. Rupture, however, may occur in the lower segment when infarction involves that area. The symptoms and signs of spontaneous rupture of a gravid uterus may vary from vague, mild abdominal pain to those of an acute abdominal catastrophe with general collapse. When the rupture is complete, fetal parts may be palpated directly beneath the abdominal wall. The accompanying abdominal distention, nausea and vomiting, and evidences of peritoneal irritation indicate the presence of an acute surgical emergency. In most cases, however, the fetus is not extruded into the abdominal cavity. Abdominal palpation usually reveals only a tender uterus, similar to moderate premature separation of the placenta. A deceptively slow decline in the level of hemoglobin confuses the diagnosis, so that laparotomy is often deferred, a delay that may prove fatal. When there is doubt, exploratory laparotomy should be done. The maternal death rate increases in direct relationship to the time elapsed between rupture of the uterus and laparotomy for the arrest of hemorrhage. Shock is not a contraindication to surgical treatment in these patients. Adequate blood replacement may mean the difference between life and death, and intra-arterial transfusion may be necessary.

Ohio State Medical Journal, Columbus

49:281-376 (April) 1953

Indications for and the Results of Surgery in Congenital Cardiovascular Diseases. S. Kaplan and J. A. Helmsworth.—p. 297.
Case of Homologous Serum Jaundice After Transfusion of Stored Whole Blood. L. B. Mehl.—p. 301.
Lesions Producing Bursitis-Like Symptoms: Importance of Radiographic Study Before Treatment of Bursitis. J. D. Osmond Jr. —p. 302.
*Anaphylactic Shock Following Administration of Penicillin. I. F. Nikishin.—p. 305.
Intramuscular Pentobarbital Sodium for Premedication to Children. J. R. Jarvis.—p. 308.
Emergency Room Treatment of Comatose Patient: Review of 100 Cases. L. V. Phillips and H. E. May.—p. 310.
Special Study of Endemic Goiter in Mexico and Central and Latin American Countries. O. P. Kimball.—p. 313.

Anaphylactic Shock Following Administration of Penicillin.—Untoward effects of penicillin are not the result of direct toxicity but of hypersensitivity. They mainly consist of urticaria, contact dermatitis, gastrointestinal reactions, arthralgia, and drug fever. Because of the antigen-antibody mechanism of penicillin reaction, as has been experimentally demonstrated, one has to be aware of a more serious reaction based on the same mechanism and known as anaphylactic shock. Nikishin found only five instances of true anaphylactic reactions to penicillin in the available literature. In reviewing the characteristics of these patients, the author says that all but one had received penicillin several weeks prior to the injection that was followed by shock, but none manifested signs of sensitivity during previous administrations. The patients received the "exciting doses" intramuscularly; intravenous injection could be proved in none of the patients. The reaction began almost immediately. It was manifested by flushing of the face, choking, wheezing, dyspnea, and a subjective feeling of tightness in the chest and throat, followed by extreme circulatory depression with a rapid, weak, almost imperceptible pulse, low or unobtainable blood pressure, profuse perspiration, and collapse. Antiallergic treatment was successful when it was employed. The author also reviews two previously reported fatal cases of anaphylactic shock follow-

ing injection of penicillin and then describes a case of his own observation, in which recovery followed various treatments. The use of drugs with antihistaminic effects proved effective in this as well as in other cases. Avoiding the allergen prevents anaphylactic shock, but an occasional inadvertent intravenous injection is apparently unavoidable. The mishap will be less frequent if the use of small caliber needles for intramuscular injections is discontinued. It seems impracticable to test the sensitivity of every patient in need of penicillin, but the author pleads for discrimination in the use of penicillin as well as other antibiotics. The duration of drug allergy is unpredictable, but may last many years and may become evident in a fatal anaphylactic shock. The number of penicillin sensitive persons is probably increasing with widening use of this powerful drug.

Pediatrics, Springfield, Ill.

11:309-424 (April) 1953

Rickets, Deficiency of "Alkaline" Phosphatase Activity and Premature Loss of Teeth in Childhood. E. H. Sobel, L. C. Clark Jr., R. P. Fox and M. Robinow.—p. 309.

Comparison of Therapeutic Efficacy of Four Agents in Pertussis. R. G. Ames, S. M. Cohen, A. E. Fischer and others.—p. 323.

Acute Nicotine Poisoning: Case Report. B. B. Oberst and R. A. McIntyre. —p. 338.

*Significance of Febrile Convulsions. W. G. Lennox.—p. 341.

Eosinophilia-Hepatomegaly Syndrome of Infants and Young Children: Report of Case Due to Invasion of Liver by Nematode Larvae. C. L. Milburn Jr. and K. F. Ernst.—p. 358.

Treatment of Meningitis with Chloromycetin Palmitate®: Results of Therapy in Twenty-Three Cases. G. E. Deane, J. E. Furman, A. R. Bentz and T. E. Woodward.—p. 368.

Pleuropneumonia Organism Meningitis Complicating Ruptured Meningocele: Report of Case with Recovery. J. H. Davis and L. H. Arnstein. —p. 381.

Staphylococcal Pneumonia and Empyema. A. Kanof, B. Epstein, B. Kramer and I. Mauss.—p. 385.

Febrile Convulsions.—Convulsive seizures that attend a febrile illness are significant because of the number of children involved. Figures from various reports and a gross estimate suggest that about 2% of all children have one or more febrile seizures in the first five years of life. Although many pediatricians believe that a fever seizure is an innocent symptom, the counterpart of a chill in an adult, Lennox feels that a febrile seizure cannot be easily dismissed. He suggests that a convulsive seizure in association with fever may mean one of six things: 1. The fever may be a consequence of a spontaneous seizure, the result of an excess of muscular energy and heat. 2. The seizure may be the result of excess hydration or of antibiotics given to combat an infection. 3. The fever may be a seizure phenomenon, the result of a paroxysmal seizure discharge in the region of the hypothalamus. 4. The seizure may be due not to the fever but to bacterial toxins. 5. It may be the secondary result of an invasion of the brain by the infectious organisms. 6. The seizure may be due to none of these, but may be the response to high fever in association with some infection. In addition, the seizure may not be the consequence of fever, but both fever and seizure may be a consequence of toxic action on brain cells. The following features have not yet been satisfactorily explained: 1. Fever-induced seizures occur mostly in the very young. 2. Almost invariably the febrile seizure is the child's initial seizure. 3. Response to fever is almost invariably a convulsion rather than some other manifestation of epilepsy. In a study of persons whose first convulsive seizure occurred during the first decade of life it was found that extreme youth and absence of pathologic changes were oftenest associated with febrile seizures. Among a total of 407 epileptics who suffered fever convulsions as the first manifestation, 76.9% subsequently experienced nonfebrile seizures. In 22% an interval of five years or longer separated the last febrile seizure from the first nonfebrile one. The fact that subsequent seizures were mostly psychomotor seizures suggests that febrile seizures may sometimes be accompanied by temporal lobe lesions. Febrile seizures are usually innocuous, but if prolonged, focal, or attended by much cyanosis or protracted coma, they may cause brain damage. Of 392 patients who sustained brain injury in the first 10 years of life, febrile seizures were blamed for the injury and the continuing epilepsy in 5.4%. The genetic influence in children having fever-induced seizures is very strong. In the author's group, this influence, as measured by the incidence of epilepsy among near relatives, is approximately double the genetic influence in young children having only nonfebrile seizures. If evidence of hereditary transmission is accepted as indicative of essential epilepsy, then a febrile seizure is epilepsy. Fever-activated epilepsy is short lived, however; the majority of children with this form had only one or two seizures.

Surgical Clinics of North America, Philadelphia

33:311-618 (April) 1953. **Partial Index**

SYMPOSIUM ON SURGERY OF CANCER

Cancer of Breast. F. E. Adair.—p. 313.

Radical Surgery in Cancer of Head and Neck: Changing Trends in Treatment. H. Martin.—p. 329.

Surgical Treatment of Carcinoma of Thyroid Gland: With Special Reference to Metastasis. W. F. MacFee.—p. 361.

*Carcinoma Involving Esophagus. G. H. Humphreys, II. and R. L. Moore.—p. 389.

Radical Surgery for Lung Cancer. W. L. Watson.—p. 401.

Diagnosis and Treatment of Mediastinal Tumors. H. C. Maier.—p. 415.

Benign Tumors of Stomach. R. Colp and V. A. Weinstein.—p. 433.

One-Stage Segmental Resection with End-To-End Anastomosis for Rectosigmoidal Cancer. G. E. Binkley.—p. 453.

Diagnosis of Biliary-Pancreatic Cancer. H. Doubilet, H. H. Sage and J. H. Mulholland.—p. 461.

Malignant Neoplasms of Spleen: Primary and Secondary. L. M. Rousselot and C. Stein.—p. 493.

Carcinoma of Bladder. W. F. Whitmore Jr. and V. F. Marshall. —p. 501.

Treatment of Malignant Melanoma of Skin. G. T. Pack, I. M. Scharnagel and D. M. Gerber.—p. 517.

Value of an Intensive Pelvic Cancer Detection Program: With Special Reference to Intraepithelial Carcinoma. M. R. Marsh and L. M. Hellman.—p. 525.

Serous Cystadenocarcinoma of Ovary: Review of 127 Cases. C. T. Javert and R. R. Rascoe.—p. 557.

Carcinoma Involving the Esophagus.—Although surgical procedures for removal of segments of the esophagus have been carried out in an increasing number of centers, with decreasing immediate mortality, few objective reports of over-all and end results are available. At the Presbyterian Hospital in New York City 228 patients with carcinoma involving the esophagus were treated in the 10 year period from 1941 through 1950. Of these, 162 had primary carcinomas of the esophagus; 47 had carcinomas of the stomach with extension to the lower esophagus; and 19 had carcinoma involving the esophagus but originating in some other structure. Most of the patients were in the sixth and seventh decades of life, and the ratio of men to women was approximately 4:1. One patient is living and apparently free of disease seven years after resection of an adenocarcinoma of the cardia involving the esophagus. No patient has survived five years after resection of a primary carcinoma of the esophagus. No patient lived more than one year after involvement of the esophagus in carcinoma originating in another structure other than the stomach. Improvements in operative techniques have resulted in substantial decrease in operative mortality during the second half of the period studied and may result in a higher proportion of long-term survivors, especially if greater selectivity is exercised in resorting to resection. Whether resection for palliation in cases with demonstrable irremovable metastases is justifiable as compared to results of radiotherapy remains in doubt. The authors feel that in order to achieve reliable evaluation of the therapeutic methods of this highly fatal disease, the results in unselected series rather than in series selected for operability should be reported.

Tennessee State Medical Assn. Journal, Nashville

46:77-120 (March) 1953

Poliomyelitis: Value of Early Diagnosis in Prevention of Paralysis. E. R. Atkinson.—p. 77.

Partial Cholecystectomy in Acute Cholecystitis. A. H. Meyer Jr.—p. 80.

Analgesia and Anesthesia with Trilene. J. R. Smith.—p. 87.

FOREIGN

Acta Allergologica, Copenhagen

6:89-160 (No. 2) 1953. **Partial Index**

Histamine Liberators and Intracutaneous Reaction to Tuberculin in Man. J. Lecomte and C. Borensztajn.—p. 89.
Serological Studies on Pollen Extracts: II. Demonstration by Serological Method of Specificity of Antigen-Mosaic of Extracts of Six Grass Pollens. M. L. Gosselin, L. S. Mynors, R. R. A. Coombs and F. H. Milner.—p. 96.
*Circulating Eosinophil Cells in Hay-Fever Patients in Relation to Specific Desensitization. P. J. Dragsted.—p. 103.
Adrenal Cortical Function in Bronchial Asthma and Its Diagnostic Value. E. Andersson.—p. 107.

Circulating Eosinophil Cells and Specific Desensitization in Hay Fever Patients.—Eosinophil counts just before and one hour after exposure to Timothy pollen demonstrated varying reactions in hay fever patients, depending on whether or not the patients had previously received specific treatment. Eleven patients who had not previously been treated and two persons allergic to fungi reacted to exposure to the specific antigen by an average increase of 46% in the eosinophil count, while 13 previously treated hay fever patients had an average decrease of 51% in the number of eosinophils. These results show that untreated and treated hay fever patients have distinctly different reactions to specific antigens in which the adrenals seem to play an important part. For the present no conclusions may be drawn as to the way in which the organism is affected by specific desensitization.

Acta Haematologica, Basel

9:201-272 (No. 4) 1953. **Partial Index**

Encephalographic and Psychologic Changes in Pernicious Anemia. W. C. L. Diefenbach, M. R. Beyers and L. M. Meyer.—p. 201.
Therapy of Symptomatic Hemolytic Anemias. K. Sievers and H.-G. Harwerth.—p. 208.
Experimental and Cytochemical Investigations on the Relations of Hemoglobin Production to Synthesis of Proteins in Erythroblastosis. S. de Carvalho.—p. 220.
*Further Studies on Blood and Bone Marrow After Administration of ACTH and Cortisone. N. G. Hävermark and N. G. Nordenson.—p. 226.
Infectious Mononucleosis with Thrombopenic Hemorrhagic Diathesis: Report of Case. J. S. Jørgensen.—p. 253.

Effect on Blood and Bone Marrow of Corticotropin and Cortisone.—Studies were made on the blood and bone marrow of three patients with arthritis who had been treated with corticotropin and cortisone. There was evidence of stimulation of the erythropoiesis and myelopoiesis, with transient reticulocytosis and an increase of the mature segmented cells. The previously inhibited maturation of the bone marrow tended to become more normal. The lymphocytes were not noticeably influenced. Continued administration of corticotropin elicited normal stimulation of the adrenal cortex, as reflected in marked eosinopenia; a slight decrease in eosinopenia was noted after treatment with cortisone. The serum iron level temporarily increased in some patients. The hyperplasia of the reticular cells of the bone marrow seemed to decrease simultaneously with a change in the phagocytosis. The lack of uniformity in the changes observed may be due to the varying dosage. The changes were less marked with cortisone, probably because cortisone affects the metabolism less than corticotropin does.

Acta Medica Orientalia, Jerusalem

12:63-94 (March) 1953

Chronic Pancreatitis: Revision of Diagnostic Criteria and Therapy. E. Lyon.—p. 63.
Urea Clearance Determination by Means of Nonprotein Nitrogen Estimation. F. Rappaport, F. Eichhorn and S. Goldberg.—p. 75.
Sarcoid of Bone Resembling Rheumatoid Arthritis: Report of Case. M. Buchmann, S. Joles and L. Nelken.—p. 80.
*ACTH Treatment in Case of Cyanide Poisoning. I. Lurie.—p. 87.

Corticotropin in Cyanide Poisoning.—The occurrence of cyanide poisoning is reported in a healthy 47-year-old man who entered by mistake a room that had not been ventilated after fumigation with hydrocyanic acid gas. The patient was given methylene blue, nitrites, and calcium thiosulfate, but did not respond. He lost consciousness and sank into deep coma. His condition improved rapidly after intravenous infusion of 25 mg. of corticotropin (ACTH). The dose was repeated after 3 hours and the patient regained consciousness after 12 hours. No explanation can be offered for the role played by corticotropin in cases of poisoning. The author believes that in the case reported the addition of corticotropin to the usual therapy played a decisive part; the prompt improvement in the patient's condition immediately after the administration of corticotropin was very impressive. There should be no hesitation in giving corticotropin a therapeutic trial in cases of severe cyanide poisoning.

Acta Neurologica et Psychiatrica Belgica, Brussels

53:247-308 (April) 1953

Functional Syndromes of the Cortex in the Region of the Middle Cerebral Artery. J. J. Lopez-Ibor and J. C. Ortiz de Zarate.—p. 247.
Symptomatology of Myoclonias. E. Krebs.—p. 268.
*Diffuse and Multiple Sclerosis. G. de Morsier and H. Feldman.—p. 279.

Diffuse and Multiple Sclerosis.—Diffuse sclerosis cannot be distinguished from the classic form of multiple sclerosis by any exact criteria, and differential diagnosis is complicated by the frequent occurrence of transitional forms. The terms diffuse sclerosis and Schilder-Foix disease are generally applied to a progressive condition found chiefly in children and young adults that is characterized by varied neurological manifestations, principally psychic disturbances, ocular signs, and those of pyramidal origin. The most striking characteristic is a primary, progressive, sclerosing process affecting the two hemispheres, either unequally or symmetrically, sparing the cortex and to a variable extent the subcortical arcuate fibers (Meynert's U-shaped fibers). The only constant abnormality in all the diseases in this group is diffuse bilateral demyelination of the oval center. Diffuse sclerosis usually progresses rapidly and remissions are rare. An unusually prolonged case of 29 years' duration was presented by a woman who was treated for pulmonary tuberculosis between the ages of 12 and 20. Lesions of the apex of the left lung necessitated a pneumothorax, after which her pulmonary condition was satisfactory. Mental disturbances, irregularities of behavior, and manual awkwardness appeared at 20; at 30, there was decided muscular weakness in the left forearm and hand, and the shock of a broken engagement to be married intensified her complaints. Her walk became ataxospasmodic about 10 years later and her mental condition deteriorated still further; at the age of 50, she entered the hospital, scarcely able to walk. Her course was steadily downward and five months later she died. Autopsy showed foci of demyelination of the multiple sclerosis type. Other foci, however, resembled those found in diffuse sclerosis; demyelination was irregular and predominantly hemispheric, cells containing granulolipid bodies were present, and there was marked perivascular lymphocytic infiltration.

Acta Tuberculosea Scandinavica, Copenhagen

28:1-154 (No. 1-2) 1953. **Partial Index**

*Tuberculosis in Bornholm After B.C.G. Vaccination. H. C. Olsen.—p. 1.
Rehabilitation. F. Heaf.—p. 31.
Extraperiosteal Plombage with Polystan Sponge: Collapse Therapy in Severe Pulmonary Tuberculosis. H. Engberg and J. L. Hansen.—p. 45.
Roentgenological Course of Cavity Healing. H. H. Amstein-Langaas.—p. 62.
Problems Concerning Demonstration of Tubercle Bacilli in Gastric Lavage. I. H. C. Engbaek.—p. 74.
Position of Lymphoglandular Bronchial Tuberculosis in Tuberculosis Infection. R. H. Dahl.—p. 100.

Tuberculosis in Bornholm After BCG Vaccination.—Changes are reported in the incidence of tuberculosis among the population of the Danish island of Bornholm in the Baltic sea under steadily increased BCG vaccination. Between 1936 and 1940 the first mass examinations were carried out of persons up to the age of 35 years. These studies revealed that persons with a negative tuberculin reaction were predisposed to infection. As the island population became more and more tuberculin-negative, it was decided in consultation with the Danish State Serum Institute, to begin propaganda in favor of increased BCG vaccination. Between 1941 and 1945 extensive vaccination

was carried out in the schools. By the end of 1945 about 23% of the entire population had been vaccinated. Most of the vaccinated persons were between the ages of 7 to 20 years. As a result of this increased BCG vaccination the incidence of tuberculosis has decreased perceptibly. At the same time the number of persons whose reactions reverted from positive to negative increased, including persons with a natural positive reaction and those with a BCG-induced positive reaction; this situation necessitated an increasing number of revaccinations. BCG vaccination also changed the age distribution curves of newly reported cases of tuberculosis, so that the former peak at about the age of 20 has now been entirely leveled off. To make the BCG vaccination as widespread as possible, a second mass examination was carried out in 1946 and the entire population above school age were invited to attend. By the end of 1946 a total of 17,563 persons or 33.9% of the population had been vaccinated. Statistical data showed that the annual rate of infection per hundred per year of observation is only 2.5 and that the duration of BCG immunity ascertained by positive reactions to tuberculin drops slowly in the course of years, particularly during the first postvaccination years. New cases of tuberculosis and deaths from the disease are most frequent among persons with negative reactions and less frequent among those with positive reactions, but the incidence of new cases is lowest among those who had been vaccinated with BCG. Between 1946 and 1948 Bornholm fishermen had been catching salmon along the coast of Poland where they made contact with a highly tuberculous population. Two of these fishermen who had a negative reaction to tuberculin and had not been vaccinated were infected. On their return to Bornholm they passed the infection on to younger unvaccinated members of the family, with the result that nine cases of tuberculosis occurred in the course of two years. A similar tuberculous infection in Norwegian fishermen passed on in some Norwegian parishes where BCG vaccination had not been carried out spread widely, with hundreds of persons being infected in a short time. Tuberculosis in Bornholm is on the decline. Immunity in the population will be maintained by continuing with widespread BCG vaccination. Today Bornholm has 48,000 inhabitants and 49.6% of them had been vaccinated with BCG up to the end of 1950. Since 1949, examinations by age groups of 1, 7, 13 and 25-year-old persons have been done by the Bornholm tuberculosis dispensary. In addition all those taking up residence in the island are examined. Each examination consists of a tuberculin test followed by BCG vaccination of all those with a negative reaction, and x-ray screening of all school children and adults with a positive reaction. In addition, systematic examinations of adolescents attending schools, of men in the armed forces, seamen, and school teachers and the now compulsory examination of apprentices are continued. It is hoped that by this method the rate of the infection will be further reduced and at the same time the immunity among the population increased.

Archiv f. Orthopädische und Unfall-Chirurgie, Munich

45:415-562 (April 15) 1953. **Partial Index**

Endogenic Causes of Vertebral Osteochondrosis of the Lumbar Region. H. Erdmann.—p. 415.
Treatment and Evaluation of Sudeck's Syndrome. C. Blumensaat.—p. 451.
*Pathogenesis of Sudeck's Syndrome. K. H. Hackethal.—p. 482.
Surgical Treatment of Irreducible and Old Dislocations and Dislocation: Fractures of the Shoulder Joint. H. Platzgummer.—p. 514.
Endoprostheses of Methyl Methacrylate for Hip-Joint: Operation and Results. O. A. Stracker.—p. 522.
Treatment of Congenital Dislocation of Head of Radius. H. Detzel.—p. 536.
Osteopathia Patellae Juvenilis: Two Cases. H. Classen.—p. 543.

Pathogenesis of Sudeck's Syndrome.—The dystrophy of an extremity, first described by Sudeck in 1900, was later designated as Sudeck's syndrome. According to Hackethal various theories have been advanced to explain the pathogenesis of this syndrome, and the two most widely accepted at present are: the reflex theory of Vulpian-Charcot and the peripheral humoral theory of Rieder. The author feels that neither of these, nor various other theories are entirely satisfactory. On the basis of observations on 27 cases of Sudeck's syndrome of the upper extremity, the author regards the syndrome as the terminal stage of a neurodystrophic process. This neurodystrophic theory explains Sudeck's syndrome as the direct result of a serious dissociated irritation and paralysis of the nerve fibers of a certain area. The most common, but by no means the only cause is nerve strangulation, particularly strangulation of the nerve root. The hub of this process is the spondylogenic nerve root irritation, that is, mechanical root irritation produced by a disproportion between the size of the vertebral foramen and the nerve root diameter. The relative stenosis of the vertebral foramen is an important predisposing factor; and an ascending neuritis is probably the most important factor in the development of Sudeck's syndrome. The author considers causalgia as an especially severe form of Sudeck's syndrome, which is probably most often produced by massive nerve compression.

Archivos de Pediatría del Uruguay, Montevideo

24:73-132 (Feb.) 1953. **Partial Index**

Value of Sodium Salicylate in Prevention of Heart Diseases in Rheumatic Fever. D. Barbato.—p. 73.
*Acute Porphyria: Case. C. A. Escande, C. Boccoleri, R. García Güelfi and L. E. Folle.—p. 83.

Acute Porphyria.—Acute porphyria in children is extremely rare. The authors report a case in a girl who was apparently normal until the age of 12, when she complained of lumbosacral pain and redness of the urine. A clinical diagnosis of acute porphyria was confirmed by the positive results of fluoroscopic and spectroscopic examination of the urine for porphyrins. The early symptoms were followed by abdominal pain and in two weeks by an ascending Landry's paralysis, which progressed to diaphragmatic paralysis. The latter was controlled by the use of the iron lung for 5 days on one occasion and for 35 days on a second occasion. After a stormy course, the symptoms regressed slowly. Cure with complete muscular recovery was obtained in a year. Porphyrinuria was revealed in the father and three out of five siblings of the patient by fluoroscopic examination. According to the authors, porphyria is a hereditary disorder of the metabolism of porphyrins that can be either latent in the form of porphyrinuria or else develop into the cutaneous or the acute forms of the disease. The cause of the metabolic disorder is unknown. The treatment is symptomatic. The authors advise physical and mental rest, an antiallergic diet, administration of 100 to 200 mg. of nicotinic acid amides by mouth daily, daily intramuscular injections of 5 cc. of raw liver extract, use of antibiotics if infections, especially respiratory infections, occur, and administration of calcium gluconate in daily doses of 1 or 2 gm. by intramuscular route. The authors do not specify the duration of the treatment. The use of the iron lung is indispensable in disorders of respiration of neurological origin. Sulfonamides and corticotropin (ACTH) aggravate this disease.

Ärztliche Wochenschrift, Berlin

8:345-376 (April 10) 1953. **Partial Index**

*Clinical Experiences with Treatment of Coronary Insufficiency with Crystalline Visammin Compared to the Efficacy of Nitrite and Theophylline Preparations. A. H. Lemmerz and J. Kranemann.—p. 350.
Comparative Study of Behavior of *p*-Aminosalicylic Acid and Isoniazid During Gestation and Lactation in Experimental Animals. H.-D. Renovanz and K. Schattmann.—p. 354.
Clinical Experiences and Paper-Electrophoretic Study of Serum Proteins in Tuberculous Patients Treated with Vitamin T. E. Lucas and A. Schmager.—p. 359.

Crystalline Visammin in Coronary Insufficiency.—Of 500 men with coronary insufficiency, 50 who did not respond satisfactorily to treatment with nitrites and theophylline compounds were given crystalline visammin (khellin) orally in doses varying from 60 to 300 mg. daily. In 25 of these the insufficiency was characterized predominantly by symptoms of generalized vascular sclerosis; in 19 autonomic disturbances were manifested by the altered dermographic latent period, increased reflexes, and tendency to sweating, which indicated a definite deviation of the vegetative tonus to the vagotonic or sympatheticotonic side. The remaining six patients had cardiac decompensation due to angina pectoris. In the group with predominantly sclerotic symptoms, the optimal dose of the

drug seemed to be about 120 mg. per day, which was adequate to render 11 patients free of complaints. The one definite therapeutic failure in this group was a patient with irritation of the pleura. Apparently the irritated pleura maintained the coronary disturbance through viscerovascular reflexes. Fifteen of the 19 patients with disturbance of the autonomic nervous system obtained good results, while 4 were therapeutic failures. In three of the latter pronounced hypotonic orthostatic disturbance was demonstrated by the electrocardiogram made in standing position and by Schellong's experiment. Kymographic recordings showed a pronounced contractile dysfunction of the heart in the fourth patient. Three of the six patients with cardiac decompensation responded satisfactorily to crystalline visammin. One patient with a combined aortic-mitral lesion had been refractory to treatment with Convallaria majalis for two weeks, and another with aortic valve insufficiency had not responded to previous treatment with a proprietary squill glycoside preparation for 17 days. The third patient with a left bundle branch block on a sclerotic basis responded to the small dose of 0.12 mg. of strophanthin combined with 200 mg. of crystalline visammin. The other three patients were therapeutic failures, probably because the dose was too small. The number of patients with cardiac decompensation due to angina pectoris is too small to draw conclusions concerning the glycoside-reducing effect of crystalline visammin that has been observed in three of these patients. Results obtained in the other two groups showed that improvement may still be obtained with crystalline visammin in many patients in whom nitrites or theophylline preparations are ineffective. Even doses as large as 300 mg. were well tolerated. Because of its almost specific spasmolytic effect on the smooth muscles of the coronary vessels, crystalline visammin is contraindicated in orthostatic disturbance of circulation, the symptoms of which depend on the failure of reflex-controlled capacity of circulatory adaptation but not on the spasm.

British Heart Journal, London

15:113-272 (April) 1953

Radiological Diagnosis of Rheumatic Pericardial Effusion. E. M. M. Besterman and G. T. Thomas.—p. 113.

*Incidence and Life Expectation of Children with Congenital Heart Disease. B. MacMahon, T. McKeown and R. G. Record.—p. 121.

Multi-Channel Cathode-Ray Phonocardiograph. E. M. M. Besterman and J. K. Harrison.—p. 130.

Opening Snap of Mitral Stenosis. P. Mounsey.—p. 135.

Caval Refluxes in Angiocardiography and Dynamics of Right Atrium. C. Hedman, J. Lind and C. Wegelius.—p. 143.

Anomalous Right Subclavian Artery. J. N. Pattinson.—p. 150.

Innervation of Heart. G. A. G. Mitchell.—p. 159.

Paroxysmal Ventricular Tachycardia: Clinical Classification. R. Froment, L. Gallavardin and P. Cahen.—p. 172.

Congenital Aortic Valvular Stenosis. M. Campbell and R. Kauntze. —p. 179.

Paroxysmal Tachycardia in Pregnancy. P. Szekely and L. Snaith.—p. 195.

Cardiovascular Disease in Random Sample of Elderly People. H. Droller and J. Pemberton.—p. 199.

Comparison of Operation and Clinical Findings in Mitral Stenosis and Incompetence. A. Venner and H. E. Holling.—p. 205.

Gross Calcification of Mitral Valve. A. Wynn.—p. 214.

Mechanisms of Adaptation to Central-Venous-Arterial Shunt. P. H. Davison, G. H. Armitage and W. M. Arnott.—p. 221.

Phaeochromocytoma. M. Hamilton, J. W. Litchfield, W. S. Peart and G. S. C. Sowry.—p. 241.

Atrial Electrogram in Mitral Stenosis. G. Reynolds.—p. 250.

Life Expectation of Children with Congenital Heart Disease.—An attempt has been made to obtain information on all cases of congenital heart disease in children born in the years 1940-1949 to mothers residing in Birmingham, England. In 199,418 there were 633 cases of congenital heart disease. Diagnosis was confirmed at necropsy in 236, at operation for patent ductus arteriosus in 19, and by a consultant physician in 223. In the remaining 155, the diagnosis depended on the report of the school medical officer in 10 or on certification of the cause of death in 145. The 633 cases of congenital heart disease represented an incidence of 3.17 per thousand total births, and 3.23 per thousand live births. For the years 1940 to 1944, when ascertainment was more complete than in later years, the incidence was 3.62 per thousand total births and 3.73 per thousand live births. Estimation of life expectation at birth suggests that of 10 children with congenital heart disease born alive, 2 die by the end of the first week, another 1 or 2 by the end of the first month, and another 2 by the end of the first year. Between three and four survive to the 10th birthday. For the purpose of considering the frequency of association between malformation of the heart and other congenital malformations, the 145 cases recorded from the death register were excluded because of incomplete data. In the remaining 488, associated abnormalities were observed in 101 (21%). Thirty-one of these had mongolism. Of 18 with mongolism in whom the nature of the heart lesion was known, 14 had septal defects. Except for mongolism there was no noteworthy association of congenital heart disease with any other single malformation. Of the 633 children with congenital heart disease, 338 (53%) were boys. The percentages of males with various types of cardiac malformations were as follows: transposition of great vessels 72%, persistent common truncus arteriosus 47%, pulmonary stenosis 69%, coarctation of aorta 44%, septal defects 55%, and patent ductus arteriosus 39%. A slight predominance of men over women has generally been reported in the literature in series of grouped congenital heart defects.

British Journal of Industrial Medicine, London

10:69-140 (April) 1953

Respirators for Protection Against Mercury Vapour. V. B. Vouk, Z. Topolnik and M. Fugaš.—p. 69.

Action of Flint of Variable Size Injected at Constant Weight and Constant Surface into Lungs of Rats. E. J. King, G. P. Mohanty, C. V. Harrison and G. Nagelschmidt.—p. 76.

Dust Sampling to Simulate Human Lung. H. H. Watson.—p. 93.

Pneumoconiosis of Coal Miners in Scotland. J. Black.—p. 101.

Pilot Investigation into Occurrence of Pneumoconiosis in Large Power Stations in South Wales. I. Davies.—p. 111.

Expected Frequency of Bladder Tumour in Works Populations. R. A. M. Case.—p. 114.

Methyloctylbenzenesulphonate: New Industrial Sensitizing Agent. C. N. D. Cruickshank and H. Howard-Swaffield.—p. 121.

Psychological Handicap in Relation to Productivity and Occupational Adjustment. M. Markowe and L. E. D. Barber.—p. 125.

British Journal of Plastic Surgery, Edinburgh

6:1-72 (April) 1953. **Partial Index**

*Fate of Preserved Bovine Cartilage Implants in Man. T. Gibson and W. B. Davis.—p. 4.

Preliminary Report on Use of Preserved Homogenous Cartilage Implants. A. L. Schofield.—p. 26.

Oro-Antral Fistula. E. Peet.—p. 32.

Treatment of Ulceration of Legs by Physiotherapy. I. M. Curwen. —p. 41.

Lymphangioma of Tongue. F. Robinson.—p. 48.

Control of Extensive Burns. A. D. R. Batchelor.—p. 57.

Fate of Preserved Bovine Cartilage Implants in Man.—Gibson and Davis began to use implants of ox cartilage tentatively in 1948. The cartilaginous part of an ox scapula was obtained fresh from the slaughterhouse, cleaned of soft tissues and perichondrium, and cut into pieces of suitable size. It was then immersed in 1:4,000 thimerosal (Merthiolate) solution, which was slowly heated to the boiling point and maintained there for 10 to 15 minutes; the cartilage was found to warp badly if boiled rapidly. It was refrigerated until needed. At first ox cartilage seemed an excellent material either for skeletal support or for building up contours. No immediate reaction was seen in the tissues, and in only one case was the implant lost from sepsis, which was due to partial necrosis in the overlying flap. As time passed it was noted that most of the implants showed signs of absorption, and after 18 months some had disappeared completely. This progressive absorption of the bovine cartilage implants was also noted by other observers. Recently the authors made a follow-up study on 18 patients in whom they had used implants of bovine cartilage. Four patients could not be traced, in one the implant was lost early from sepsis, and one nasal implant was removed after three months and replaced by bone because the cosmetic result was unsatisfactory. Ten of the remaining 12 implants had been absorbed within two years. A second surgical implant in one case was found to be destroyed more rapidly than the first. Experimental implants in this case compared with controls showed on histological examination that a very marked sys-

temic response to bovine cartilage had developed. This suggests that an antigen-antibody reaction might be responsible for the absorption. Experiments in human volunteers demonstrated that each successive implant showed greater absorption than the preceding one. Absorption occurs first by surface erosion, then by fibrous replacement, and later by dissolution of the cartilage, as the host's reaction increases. The antigenic activity of this relatively insoluble material is related to its surface area. The long survival of block implants, e. g., in a nasal bridge, is considered to be due not only to their relatively small surface area but also to their fibrous encapsulation. The observation that bovine cartilage of one batch may be absorbed much more rapidly than that of another to which the body has not become accustomed raises the question of whether the antibody is specific for a single breed of cattle or even for a single animal. Results in plastic surgery with bovine cartilage are likely to be disappointing.

British Journal of Tuberculosis, London

47:65-120 (April) 1953. **Partial Index**

Tuberculin Test: Comparison Between Jelly and Mantoux Tests. H. W. O. Frew, J. R. Davidson and J. T. W. Reid.—p. 68.
Pulmonary Sequelae of Enormous Dilatation of Left Auricle. N. H. Schuster.—p. 73.
Unusual Type of Reaction to P.A.S. with Review of Its Toxic Effects. J. Evans.—p. 78.
Friedländer Lung Abscess: Treatment by Early Surgical Drainage. K. M. Shaw.—p. 84.
Angiocardiography in Relation to Intra-Thoracic Disease. J. F. Goodwin and R. E. Steiner.—p. 89.
Chronic Disseminated Tuberculosis: Report of Two Cases. P. M. Ward. —p. 94.
Carcinomatous Infiltration of Wall of an Extra-Pleural Space, with Special Reference to Pathogenesis. P. E. Baldry.—p. 98.
*Thoracic Duct Fistula Following Thoracoplasty: Report of Case. C. Cummins.—p. 101.
Polycythaemia Vera in Chronic Pulmonary Tuberculosis. P. Ellman and A. C. Fairburn.—p. 107.

Thoracic Duct Fistula.—Cummins reports the case of a woman, aged 45, with a normal convalescence following a thoracoplasty until the eighth postoperative day, when the wound was exposed for the removal of stitches. The wound was found to be elevated by a long, curved, sausage-shaped tumor that was fluctuant. Aspiration revealed a milky fluid, which was confirmed as chyle. A similar fluid was obtained by aspiration of Sembs' space anteriorly through the bed of the resected first rib. It was apparent that the thoracic duct had been injured during the apicolysis. About 30 oz. (940 cc.) of chyle were removed at the first aspiration. Daily aspirations of the wound region and Sembs' space were instituted, and the second stage of the operation was postponed. During the succeeding 13 days some 260 oz. (13 pt. or 6.1 liters) of chyle were removed by aspiration. At the second operation (three weeks after the first) about 1 qt. (1 liter) of chyle were evacuated; when the region of the fistula was mopped dry, the leak was apparent at the level of the arch of the aorta. Dissection revealed a complete tear of the main thoracic duct, with chyle dripping from the torn end of the caudal segment at the rate of 30 drops a minute. The leaking end of the duct was isolated and ligated, but a search for the other torn end was unsuccessful. The author believes that a shorter rather than a longer period of conservative treatment in the form of aspiration and diet is preferable in cases of chylous fistula. While no rigid rules can be laid down, the production of half a pint or more a day over a period of three weeks would seem to indicate that surgical intervention should be undertaken. Anastomosis to a vein has been successfully performed in some instances. Anastomosis of the cut ends of the duct or repair of the wall is also feasible, but these methods may be technically impossible as well as unnecessarily complicated. Tamponade of the region of the fistula may be required if the cut ends of the duct cannot be located. Since the thoracic duct has innumerable collateral communications with the lumbar intercostal and azygos veins, it has been suggested that the main duct should always be ligated in addition to any local treatment of the tributary. The third available procedure is ligation. This is the simplest method, and in the reported case proved to be effective.

British Medical Journal, London

1:847-896 (April 18) 1953

Magic, Medicine, and Religion: Persistence of an Idea. S. Smith.—p. 847.
Role of Adrenal Cortex in Fluid and Electrolyte Metabolism. F. T. G. Prunty, H. E. M. Kay, G. de J. Lee and R. R. McSwiney.—p. 852.
*Benign Form of Acute Osteitis of Spine in Young Children. A. E. Bremner and G. A. Neligan.—p. 856.
Pathogenesis of Hodgkin's Disease. M. H. Gordon.—p. 860.
Pubertas Praecox Caused by Interstitial-Cell Tumour of Testicle. J. Anagnostou and G. J. Frangopoulos.—p. 861.
Cerebrospinal Fluid Pressure. D. Bowsher.—p. 863.
Transverse Arrest of Head and Occipito-Posterior Position. B. Williams. —p. 865.
Subarachnoid Haemorrhage in Pregnancy. J. N. Walton.—p. 869.

Benign, Acute Osteitis of Spine in Children.—Bremner and Neligan observed seven young children with low-grade pyogenic osteitis of the lumbar spine. At the onset there were symptoms of a mild or moderate febrile illness and of a spinal lesion. Irritability, loss of appetite, and feverishness were noticed in most of the cases. Previously active children had stiff backs and spasms of pain and later objected to sitting or walking or even to being handled. These symptoms increased very gradually for up to five or six weeks and then became stationary or began to improve. The four children with the "hip syndrome" had a well-marked limp at the onset or within the first two weeks of illness. At the onset the ages of the patients ranged between 9 months and 2½ years. X-ray films of the lumbar spine showed narrowing of a disk space, with erosion of the adjacent margin of the body of either or both of the vertebrae bounding it. In one case there was also a posterior displacement of the upper of the two affected vertebrae. In two other cases the anteroposterior view showed an angular scoliosis at the level of the lesion. The children were treated by rest in a plaster bed; one patient was given penicillin in addition. They were allowed up without restriction of activity after periods ranging from 7 to 22 weeks. All remained well after follow-up periods of from 4 to 16 months. There is circumstantial evidence to suggest that the lesion is due to staphylococcic osteitis. The clinical picture strongly resembles that of tuberculous spondylitis. The distinction may be made by the tuberculin skin test, and be confirmed by the appearance of recalcification in the x-ray films within three months of the onset in the pyogenic cases. These children should be immobilized during the active stage of the disease, but activity can be permitted as soon as roentgenograms reveal recalcification.

1:897-952 (April 25) 1953

Hazards of Pregnancy in Women with Heart Disease. C. Bramwell. —p. 897.
Treatment of Genito-Urinary Tuberculosis: Further Report. J. C. Ross, J. G. Gow and C. A. S. Hill.—p. 901.
Significance of Thyroid in Psychiatric Illness and Treatment: Routine Examination with Radioactive Tracer Method. M. Reiss, R. E. Hemphill, R. Maggs and others.—p. 906.
Anticoagulants in Myocardial Infarction. I. S. L. Loudon, J. C. Pease and A. M. Cooke.—p. 911.
Rupture of Heart as Result of Br. Abortus Endocarditis. G. H. Grant and C. L. Stote.—p. 914.
*Observations on Gold Therapy in Rheumatoid Arthritis. R. A. P. Brown and J. P. Currie.—p. 916.
Disseminated Aspergillosis and Moniliasis Associated with Agranulocytosis and Antibiotic Therapy. N. E. Rankin.—p. 918.
*Monilia Peritonitis. P. C. Reynell, E. A. Martin and A. W. Beard. —p. 919.

Gold Therapy of Rheumatoid Arthritis.—Brown and Currie report studies of 220 arthritic patients, 38 of whom were treated with gold. Sixty were treated with copper, 60 with isotonic sodium chloride solution, 21 with arsenic, 22 with physiotherapy, and 19 with acetylsalicylic acid. The courses lasted 13 weeks. Diagnosis of rheumatoid arthritis was based on the criteria of polyarthritis, radiological confirmation or lack of evidence of other joint diseases, normal uric acid content of the blood, negative Wassermann reactions, negative gonococcal complement-fixation tests, negative serum agglutination test for brucellosis, acceptable clinical history and picture, increased erythrocyte sedimentation rate, and increased plasma viscosity. The patients were assessed for improvement at the end of the course, three months later, and one year after treatment. Subjective improvement was based on pain, performance, well-being, and appetite; objective improvement

was assessed by joint measurements, erythrocyte sedimentation rate, plasma viscosity, and degree of anemia. The results obtained indicate that the effect of a single course of treatment with gold salts was no better than that of the other methods described.

Candida Peritonitis.—A man was hospitalized with foot-drop, fever, and abdominal pain. Later a wrist-drop developed, and signs of active carditis appeared. Studies did not reveal the cause. Penicillin was given, but bronchopneumonia developed. Because the patient was thought to have polyarteritis nodosa and despite the fact that he was known to have duodenal ulcer, he was treated with 100 mg. of corticotropin and 2 gm. of aureomycin daily. After three days of this regimen he complained of severe abdominal pain and his abdomen became distended. His condition did not permit surgical intervention, but 60 oz. (1.7 liters) of brownish viscid fluid was aspirated from the peritoneal cavity. Administration of corticotropin was stopped, and the stomach was aspirated. Dextrose in isotonic sodium chloride solution was given by the drip method and oxytetracycline (Terramycin) was also given intravenously. Three days later 100 oz. (2.8 liters) of fluid were withdrawn by paracentesis. Large numbers of Candida organisms were found on direct examination of the fluid, and a pure growth of Candida albicans was obtained on culture. Gentian violet was given daily by intraperitoneal injection. The patient died four days later. Necropsy revealed a perforated ulcer in the first part of the duodenum. The aureomycin must have altered the intestinal flora until C. albicans was dominant; when the ulcer perforated as a complication of treatment with corticotropin, this organism obtained access to the peritoneal cavity and set up the infection.

1:953-1006 (May 2) 1953

Combined Chemotherapy in Bacterial Infections. L. P. Garrod.—p. 953.

Clinical Trial of New Oral Diuretic. A. G. Spencer and H. G. Lloyd-Thomas.—p. 957.

Controlled Hypotension in Neurosurgery with Hexamethonium and Procaine Amide. D. Aserman.—p. 961.

*An Outbreak of Diphtheria: Influence of Immunization. C. D. L. Lycett and J. T. A. George.—p. 964.

Pigmented Scars. B. S. Crawford.—p. 969.

Analysis of 50 Cases of Persistent Ductus Arteriosus. F. Starer.—p. 971.

*Reduction of Post-Operative Pain. D. L. Lewis and W. A. L. Thompson.—p. 973.

"New" Rh Antibody Anti-f. R. E. Rosenfield, P. Vogel, N. Gibbel and others.—p. 975.

Three Cases of Suppuration Due to Fusiformis Infection. W. M. R. Henderson.—p. 975.

Experiment to Determine if a Proguanil-Resistant Strain of P. Falciparum Would Respond to Large Doses of Pyrimethamine. S. A. Jones.—p. 977.

Diphtheria and Immunization.—An outbreak of diphtheria caused by Corynebacterium diphtheriae gravis in the urban district of Coseley and the surrounding districts of the administrative county of Stafford, England, is reported. There were 108 cases with 6 deaths during 1951 in a population of 267,250. An additional 31 persons were found to be harboring the pathogenic agent. In Coseley there had been for some years an incidence of diphtheria unusual in England since immunization became general. The outbreak was provided with fertile soil by the low level of immunity of the child population, and was not the result of development of a strain of C. diphtheriae gravis more than usually capable of overcoming the immunity produced by the ordinary diphtheria antigens. Long-term carriers appeared to play no part in the spread, and the large numbers of persons harboring the organism with slight or no symptoms were probably subclinical cases or transient carriers, being the result and not the cause of the outbreak. The infection was probably spread mainly at home rather than at school, although most of the cases were in school children. No explanation could be offered for the remarkable grouping of confirmed cases and of persons found to be harboring the organism in certain areas of Coseley. In the two districts most affected the incidence dropped immediately after mass immunization of the school population. The outbreak emphasized the importance of a constant watch on the proportion of children receiving reinforcement doses of diphtheria antigen, and showed that reliance on the figures prepared for the annual immunization return may be misleading, especially where school children are concerned. The outbreak occurred in an area in every district of which at least 73% of the school population had completed a course of immunization at some previous time. Although 49.1% of all the confirmed cases had some history of immunization, only 12% had been protected adequately within the preceding three years. Of the 22 patients with severe disease, only 7 (31.8%) had any history of immunization at all. Five of the six patients who died had never been immunized, while the sixth, an 8-year-old girl, had only a doubtful history of immunization in infancy. Thus further evidence was provided for the belief that the risk of severe illness or death is reduced for those who have at any time been immunized. The outbreak also demonstrated the greater willingness of the public to accept immunization when they are confronted with an outbreak of diphtheria.

Reduction of Postoperative Pain.—Pain is the chief factor preventing full respiratory excursions and adequate coughing after abdominal operations. In 30 patients between the ages of 31 and 78 who underwent abdominal operations with upper paramedian incisions, 4 cc. of a 2% solution of procaine hydrochloride was injected after closure of the peritoneum and before the patient left the operating room into the rectus sheath through polyethylene tubes, and 3 to 5 cc. of the same solution was injected by the same route every three hours for the next three days. All of the patients had considerable relief from pain a few minutes after the injection was given. The patients were able to carry out their breathing exercises unhampered by pain, movement in bed was facilitated, and ambulation was made more comfortable. Some patients found that passage of urine and flatus was much easier after the injections. There was no delay in healing or any evidence of wound infection. The necessity for postoperative narcotics was greatly diminished, and the incidence of postoperative pulmonary morbidity was reduced. The method was also found to be successful in midline incisions, the tubes being placed between the peritoneum and the linea alba.

Canadian Medical Association Journal, Montreal

68:423-530 (May) 1953

Hydatid Infection in Canada. M. J. Miller.—p. 423.

Experience with Anticoagulant Therapy in Treatment of Coronary Thrombosis. J. A. Lewis.—p. 434.

Studies on Poliomyelitis in Ontario: VI. Additional Laboratory Studies on Cases of Clinical Poliomyelitis Excreting Coxsackie Virus. A. J. Rhodes, E. M. Clark, W. Wood and others.—p. 438.

Malaria in Korean Veterans. T. R. Hale and G. W. Halpenny.—p. 444.

*An Epidemic of Acute Nephritis. R. W. Reed.—p. 448.

Haemolytic Disease of Newborn. B. P. L. Moore.—p. 455.

Complications and Dangers of Radium and X-Rays in Gynaecological Conditions. F. Batley.—p. 460.

Mysoline, a New Anticonvulsant Drug: Its Value in Refractory Cases of Epilepsy. B. H. Smith and F. L. McNaughton.—p. 464.

Relationship of Physiotherapy to Occupational Therapy in Rehabilitation. A. Zinovieff.—p. 468.

Role of Physiotherapy in Pre- and Post-Operative Care. M. Minuck.—p. 471.

Public Health and Head Injuries (Due to Road Accidents). H. Elliott and H. L. Roundthwaite.—p. 475.

Chronic Relapsing Pancreatitis with Carcinoma of Head of Pancreas. M. G. Israels.—p. 480.

Use of Corticotropin and Cortisone in Dermatology. W. S. Maddin and J. L. Danto.—p. 483.

Epidemic of Acute Nephritis.—An outbreak of acute nephritis in a sharply localized rural area is reported. Twenty-one of 22 cases of typical nephritis reported during the period from November, 1951, to February, 1952, were in persons under 17 years of age. There were two deaths from uremia. School and family illness records showed a very high incidence of sore throat during the winter. Throat cultures on 153 persons one month after the last reported cases of nephritis yielded 53 strains of hemolytic streptococci belonging to Lancefield's group A, Griffith's type 12. Carrier rates in the school and family groups were four times as high for those less than 17 years old as for the older group. These rates corresponded well with the incidence of nephritis and sore throat in the two groups over the winter period. Determinations of antistrepto-

lysin O titers indicated recent infection with streptococci in most of those tested. The data presented lend weight to the generally held opinion that hemolytic streptococci play a part in the development of acute nephritis.

Cuore e Circolazione, Rome

37:1-64 (Feb.) 1953. **Partial Index**

Diagnosis of Atrial Flutter by Means of Graphic Method. S. Contro. —p. 1.
*Late Results of Pneumopericardium in Treatment of Exudative Pericarditis. G. Russo.—p. 14.

Late Results of Pneumopericardium in Exudative Pericarditis.—Late results are reported in seven cases of exudative pericarditis treated with pneumopericardium. Clinical, roentgenological, and electrocardiographic studies were made in four cases from 1 to 11 years after the treatment. Two patients who could not be seen because of a great traveling distance have confirmed by mail that they are well, and one died of acute miliary tuberculosis. The patients' ages at the time of treatment ranged from 15 to 63 years. The exudate was removed with a 50 cc. syringe to assure a slow removal and substitution of the gas for the exudate as this was being removed. In some cases the syringe was left in place for some time to permit complete emptying of the pericardiac cavity and to prevent even the temporary fusion of the pericardiac sheaths. The quantity of gas injected was individualized in each case, and attempts were made to establish a balance between the intrapericardiac and the atmospheric pressure. To prevent adhesive pericarditis, the injection of gas into the pericardium was continued long after all the exudate was removed, namely, until the clinical and roentgenological examinations indicated that the evolutional process was stopped and the inflammation had completely subsided. All the patients tolerated the treatment well, and there were no untoward effects to contraindicate continuation of the treatment. After the first tapping, there was always an improvement in the circulation, with decreased tachycardia, reduction or disappearance of dyspnea and precordial distress, and progressive decrease in the size of the liver. The drop in the venous pressure was always proportional to that in the pericardiac pressure. From five to eight tappings were sufficient for six patients. The other was a 22-year-old man who was hospitalized for one year and needed 58 tappings for removal of about 13 liters of exudate. After each tapping, 220,000 units of penicillin were introduced into the pericardium. At the time of writing three years later, the patient was well and had resumed his job as a carter. Streptomycin was used locally in the patients who were treated in the antibiotic era. This drug was given systemically with *p*-aminosalicylic acid to the patients with tuberculous forms and with sodium salicylate to those with rheumatic forms. The pneumopericardium, in addition to having immediate effects on the circulation and the course of the pericardiac inflammation, prevented all the late consequences of the disease. Adhesive pericarditis was avoided in all the patients. In the four who were followed there were none of the effects that the disease produces sooner or later on the cardiovascular apparatus, and the serous pericardiac layer was completely restored to normal. The author ascribes these excellent results to the fact that the gas refills were continued until the pericardiac and parapericardiac inflammation had disappeared and clinical and roentgenological examinations revealed that the anatomic condition was again normal.

Die Medizinische, Stuttgart

15:475-530 (April 11) 1953. **Partial Index**

Diabetes Mellitus as Sequel of Trauma. A. Sturm.—p. 475.
Insulin-Creatine Therapy of Diabetic Coma. D. Jahn.—p. 486.
Fatty Degeneration of Liver and Lipotropic Substances. K. Lang.—p. 489.
Pathology of Lipoidoses: I. Cholesterosis. A. Giampalmo.—p. 492.
Cardiac Hypertrophy and Cachexia. W. Berblinger.—p. 497.
*Corticotropin (ACTH) Treatment of Agranulocytosis. H. Schulten and W. Pribilla.—p. 503.

Corticotropin Treatment of Agranulocytosis.—Two women, aged 60 and 57, and a man, aged 53, with agranulocytosis due to drug hypersensitivity were treated with antibiotics and corticotropin (ACTH). Slight improvement in the general condition had resulted in the older woman from treatment with penicillin, but there was no definite improvement in the blood count. From the 15th to the 19th hospital day the patient was given, in addition to penicillin, 50 units of corticotropin daily. In the course of this treatment the number of granulocytes increased from 440 to 1,806 per cubic millimeter of blood, while the number of leukocytes first remained unchanged. Somewhat later the blood picture was restored to normal and a clinical cure was obtained. The older woman was treated with a penicillin-streptomycin preparation (Supracillin) and with corticotropin. There was rapid improvement in the general condition and in the blood picture in the course of this treatment. In the man, rapid improvement of the general condition, with drop of temperature and an increase in the leukocytes (from 1,900 to 10,500) with 82% granulocytes, resulted from treatment with aureomycin and corticotropin (50 units daily). The authors felt that the appearance of the leukocytes in the blood of the three patients was influenced by the administration of corticotropin. The evaluation of a therapeutic procedure in agranulocytosis is made difficult by the fact that this condition tends to resolve spontaneously when treated with antibiotics. The blood picture of the three patients did not show any significant change for several days during which they had been treated with antibiotics alone. This change occurred only after the administration of corticotropin. Treatment of agranulocytosis with corticotropin alone is contraindicated by the well-known fact that corticotropin reduces the general and local resistance of the organism to infection. This effect of the hormone is particularly undesirable in agranulocytosis. Its use in combination with antibiotics is sensible in agranulocytosis because of the control of inflammation exerted by the antibiotics and the increase in the number of granulocytes in the course of treatment with the hormone. It may be lifesaving in the short critical phase of the disease.

Fortschr. Röntgenstrahlen & Röntgenpraxis, Stuttgart

78:391-530 (April) 1953. **Partial Index**

Intracranial Calcifications as Late Sequela of Tuberculous Meningitis after Treatment with Streptomycin. R. Garsche.—p. 391.
Prospects of Healing of Fractures of Vault of Cranium in Children. H.-W. Pia.—p. 396.
Roentgenologic Aspects of Lungs Following Surgery. S. Di Rienzo.—p. 400.
Technique of Bronchography in Children. P. C. Schmid.—p. 413.
*Esophageal Ulcer in Severe Kyphoscoliosis. R. Haubrich.—p. 419.
*Roentgenologic Phenomenon as Cause of Erroneous Diagnosis in Localization of Pointed Metallic Foreign Bodies in Gastrointestinal Tract. E. Kübler and S. Dortenmann.—p. 429.

Esophageal Ulcer in Severe Kyphoscoliosis.—Twenty-five patients with severe kyphoscoliosis were examined roentgenologically because of cardiac complaints or dysphagia. In two men and three women a peptic ulcer in the esophagus was detected. Esophagoscopy is not feasible as a rule in patients with severe kyphoscoliosis. In one of the five patients in whom it could be performed, it provided additional proof of the ulcer. In the remaining four patients there was no reason for proof by surgical intervention because the patients' symptoms were not suggestive of malignancy. The differential diagnosis had to be based on the roentgenologic findings alone. In most of the cases the ulcer niche could be demonstrated in a typical way as a contrast spot or by radiating folds on lateral as well as on frontal exposures. The localization of the niche always at the site of the greatest concavity was the strongest argument against diagnosis of a diverticulum. Traction diverticula of the esophagus had been described in the literature in cases of kyphoscoliotic displacement of the esophagus, but they were always observed on the convexity of the lower third, while the ulcer was found exclusively in the middle third of the esophagus. This atypical localization and the unusually high incidence of the condition are closely related. It appears very likely that the middle portion of the concavity of the considerably angular esophagus presents a site of decreased resistance that may be considered as an "esophageal channel" under mechanical stress, in analogy to the "gastric channel" and its predisposition for ulcer. Additional factors, such as a topographically conditioned disturbance of the vascular and nervous supply, incipient peptic digestion due to aberrant gastric mucosa or a rise of the

gastric juice resulting from insufficiency of the cardia, and an esophagitis associated with stenosis of the cardia, may contribute to the occurrence of the ulcer at this circumscribed weaker site of the wall much oftener than in an esophagus with a normal course.

Erroneous Roentgen Diagnosis of Gastrointestinal Perforation by Foreign Body.—Two women and a man who had swallowed a knitting needle and a sewing needle, a pin, and a nail, respectively, were examined roentgenologically to decide whether or not the pointed, metallic foreign body had perforated the wall of the gastrointestinal tract. The roentgenologic appearance suggested that in one of the women the knitting needle had perforated the wall of the stomach and the sewing needle that of the colon, and that in the other woman and in the man the pin and the nail had perforated through the wall of the stomach. Laparotomy was performed on all three patients but did not confirm the roentgenographic diagnosis. In order to explain the roentgenologic phenomenon that simulated perforation of the wall of the gastrointestinal tract in these patients, an attempt was first made to reproduce it in the stomach of human cadavers and of dead rabbits. This attempt in the atonic wall of the stomach failed. The phenomenon could, however, be reproduced in experiments made on the stomach of living rabbits. The shadows of the needles that were pressed against the inner wall of the stomach of the living animals were projected beyond the outline of the wall for as much as 1.8 cm., without, however, actually penetrating the wall; this was clearly demonstrated by use of graduated needles. The animal experiments showed that functional elements are the most important of the causes of the roentgenologic phenomenon simulating perforation, while the morphological changes in the tissues (thickening of the gastric mucosa and the finger-like extroversion of the outer layers of the gastric wall) contribute only secondarily to the clarification of this peculiar phenomenon.

Helvetica Paediatrica Acta, Basel

8:1-116 (March) 1953

Leukemia in Childhood Treated with Cortisone and Aminopterin. C. Gasser and R. Cramer.—p. 10.

Whooping Cough Vaccination and Its Contraindications. E. Köng.—p. 90.

*Bone-Marrow Culture in Purulent Meningitis. K. Choremis and T. Athanasiades.—p. 99.

Case of Acute Meningitis Caused by Moraxella Lacunata. M. Pavlatou and T. Athanasiades.—p. 104.

Myelitis After Atypical Pneumonia. R. Goldstein.—p. 107.

Arteriovenous Aneurysm of the Lung and Osler's Hereditary Hemorrhagic Telangiectasis. H. Wissler.—p. 111.

Bone Marrow Culture in Purulent Meningitis.—The valuable information provided by bone marrow culture in typhoid fever and tuberculosis led to a trial of the method in various cases of purulent meningitis. Blood, bone marrow, and cerebrospinal fluid cultures and direct smears from 56 children from 10 days to 14 years of age were studied. At least one culture proved positive in all of the 44 cases in which the specimens were taken in the first days of the disease and before antibiotics had been used. Cultures from seven patients who had had the disease for several days before admission to the hospital and who had received antibiotics were negative. Cultures obtained on the 10th hospital day from five patients who had been treated with antibiotics for approximately one week and were considered cured also proved negative. The rich vascularization of the marrow and the delayed blood flow through its sinuses make it a focus of bacterial retention in which the pathogenic agent in any blood-borne infection can be found more easily than in the peripheral blood. The percentage of positive bone marrow cultures (61.3%) among the 44 patients who had not yet received antibiotics was much higher than the percentage of positive blood cultures (34%). Cerebrospinal fluid cultures in the same patients were positive in 59%, while the direct smears were positive in 65.9%. The pathogenic agents recovered in this series included Meningococcus, Streptococcus, Diplococcus, and Hemophilus organisms.

Hospital, Rio de Janeiro

43:429-558 (April) 1953. **Partial Index**

*Incidence of Chagas' Disease in Prospective Blood Donors in Blood Bank of São Paulo City. Serologic Survey. C. de S. P. Passalacqua, V. Amato Neto, I. Zatz and A. Damasco.—p. 443.

Prostigmine and Surgery. C. de Carvalho Orecchia and D. Boechat.—p. 449.

Autositic Monphalus Sternopagus Twin Monsters: Report of a Case. F. Moreira Jr., J. Sacramento and A. Pires de Almeida.—p. 507.

Chagas' Disease in Blood Donors.—A serologic study of Chagas' disease (American trypanosomiasis) was carried out on the blood of 536 prospective donors, selected at random at the blood bank of the Santa Casa de Misericordia of São Paulo, Brazil. Most of these persons came from the rural zone of São Paulo, where Chagas' disease is endemic. The survey was followed by complement fixation tests for diagnosis of the disease. Positive results were obtained in 22 persons (4.1%). The percentage of positive results is higher than that previously reported from other blood banks of São Paulo City, probably because the test was done in blood of persons from regions where the disease is endemic. The authors point out the danger of transmission of Chagas' disease in donor blood. They urge the complement fixation test as a routine practice in blood of prospective donors, especially if they live in zones where Chagas' disease is endemic. The test should also be made in persons who had had blood transfusions on the supposition that the disease might have been transmitted through transfusion.

Lancet, London

1:755-804 (April 18) 1953

New Concepts of Poliomyelitis. P. N. Meenan.—p. 755.

Treatment of Carcinoma of Bladder. H. P. Winsbury-White.—p. 757.

Some Developments in Technique of Trigeminal Injection. J. Penman.—p. 760.

Alcohol Pain in Hodgkin's Disease. J. Bichel and P. Bastrup-Madsen.—p. 764.

*Phlebotomy for Haemochromatosis: Effect of Removing 52 Pints of Blood in 16 Months. J. C. Houston.—p. 766.

Specific Water Diuresis Test for Adrenocortical Insufficiency. S. Oleesky.—p. 769.

Parathyroid Tumour with Hyperparathyroidism and Coexistent Gastric and Duodenal Ulceration. A. Elkeles.—p. 770.

*Growth of Bacteria in Intravenous Infusion Fluids. L. Michaels and B. Ruebner.—p. 772.

Phlebotomy for Hemochromatosis.—It is known that only negligible quantities of iron can be excreted by the body, and that normally excessive absorption of iron from the intestine is prevented. In hemochromatosis there is probably a congenital defect in the mucosal block for iron. Consequently slightly more iron is absorbed than can be excreted, and the progressive accumulation of iron in the tissues is accompanied, usually at about middle age, by the characteristic pathological changes of the disease. It has been suggested that the rarity of hemochromatosis in women may be explained by the fact that iron is excreted in menstruation and pregnancy. Study of the age incidence of hemochromatosis lends some support to this hypothesis. Women get the disease later in life than men and almost always after the menopause. Investigating the ages of 202 male and 20 female patients reported on since 1935, Houston found that only two of the women were less than 45 years of age and that one of these two younger women had had amenorrhea for 13 years before dying of hemochromatosis at the age of 34. There is no way of removing iron from the body except by removing blood, which contains 500 mg. of iron per liter. A 39-year-old man with hemochromatosis proved by liver biopsy was bled by venepuncture a pint a week from Nov. 22, 1951, to July 3, 1952. Since July of 1952 a pint has been removed every fortnight. Throughout this period he has continued at work as an accountant, and at no time has he noticed any ill effects from loss of blood. To the time of writing 52 pints of blood had been withdrawn in 16 months. The author believes that such bleeding may reduce the enormous iron deposits and perhaps improve the prognosis. It might be adopted as the treatment of choice for all early cases, at least until sufficient data have been collected to enable its long-term effects to be assessed.

Growth of Bacteria in Infusion Fluids.—A dangerous reaction caused by bacterial growth in the fluid during intravenous infusion was observed by Michaels and Ruebner twice within two years. In both patients serious pyrexia developed while they received intravenous infusion therapy for several days, and in each case many coliform bacilli were found in the infusion fluid. The authors regard it as unlikely that the organisms were present in the fluid originally. In order to determine whether similar but less heavy, and therefore perhaps undetected, infection of infusion fluids occurred in hospital practice, the infusion fluids being administered to 32 patients were investigated. The fluid from the tubing was cultured within 48 hours after the infusion was begun in 19 cases, and within two to four days in 13 cases. All 32 fluids were found to be sterile. The authors also sought to ascertain whether coliform bacilli introduced into infusion fluids could multiply enough to perpetuate the contamination in the apparatus, even though a fresh uninfected bottle was substituted for a contaminated one. All the experiments were made at summer room temperature (about 20 C or 68 F). The organisms used were the coliform bacilli isolated from the aforementioned patients. It was found that considerable multiplication took place when crystalloid solutions such as Hartmann's fluid with 5% dextrose or isotonic sodium chloride solution were used, even if the bottles were changed. In cases of pyrexia of unknown origin in patients receiving intravenous therapy, a bacterial growth in the infusion set should be considered a possible cause. Attention is drawn to the importance of aseptic precautions in the administration of intravenous fluids. During a long-continued intravenous infusion the infusion apparatus and, if possible, the needle should be changed at least once every 24 hours.

1:805-860 (April 25) 1953

Normal and Pathological Physiology of Cerebrospinal Fluid Circulation. G. Schaltenbrand.—p. 805.
Effect of Isoniazid on Tuberculous Lesions of Kidneys. J. C. Dick.—p. 808.
*Isoniazid in Treatment of Female Genital Tuberculosis. T. Barns, H. G. M. Smith and L. M. Snaith.—p. 817.
Mode of Action of Tromexan. R. B. Hunter and G. R. Tudhope.—p. 821.
*Haemorrhagic Diathesis Due to Absence of Christmas Factor. S. van Creveld and M. M. P. Paulssen.—p. 823.
Cervical Aortic Knuckle Which Resembles an Aneurysm. C. Lewis and L. Rogers.—p. 825.
Case of Polyorchidism. P. St. G. Anderson.—p. 826.

Isoniazid in Treatment of Female Genital Tuberculosis.—Women with genital tuberculosis formerly received no active treatment, but since the advent of streptomycin and *p*-aminosalicylic acid, many attempts have been made to eradicate the disease with these drugs. Results have been disappointing because of the frequent reappearance of tuberculous follicles in the endometrium 6 or even 12 months after apparent cure. The effect of isoniazid alone and in combination with streptomycin and *p*-aminosalicylic acid was studied in 43 patients with tuberculous endometritis and 3 with tuberculous cervicitis; 40 showed no evidence of infection after treatment and one became pregnant. The permanence of these apparent cures can only be determined by follow-up at the end of a year or more, but the therapeutic value of the treatment is evident. The unique absence of caseation that characterizes tuberculous lesions in the endometrium probably makes them more responsive to antibiotic therapy than lesions in the fallopian tubes, where caseation is usually present. Relapse after treatment may be due to persistence of fallopian tube lesions, resulting in reinfection. All the patients received 150 mg. of isoniazid daily for 16 weeks; 11 were also given 1 gm. of streptomycin daily and 15 gm. of *p*-aminosalicylic acid daily during the last 8 weeks. No side-effects from isoniazid were noted in any of the patients, but streptomycin therapy was discontinued in one case after 30 gm. had been given, because the patient developed a rash and complained of weakness. Only four patients gained more than 4 lb. (1.8 kg.) in weight and none developed abnormal appetites. The patients were seen periodically throughout treatment, and at each visit the central nervous system was completely examined, the blood pressure and hemoglobin level were estimated, and total and differential white blood cell counts were made. No abnormalities were disclosed by any of these tests.

Hemorrhagic Diathesis Due to Absence of Christmas Factor.—The difference between Christmas disease and another hemorrhagic diathesis (hypoproconvertinemia) is illustrated by the case of a 10-year-old boy admitted to the Children's Clinic in Amsterdam. The first of many severe hemorrhages resulted from an injury at the age of 15 months, but even before this his parents had noticed that he was easily bruised. He was found to have a prolonged coagulation time and a diagnosis of hemophilia was made. His parents were healthy and no trace of a hemorrhagic diathesis could be found in the family. Tests on admission showed a greatly prolonged venous clotting time; normal bleeding time, clot retraction, fibrinogen content, and thrombocyte count; normal capillary resistance; and insufficient prothrombin consumption on coagulation. Various factors contradicted the diagnosis of hemophilia: 1. The patient's plasma in various dilutions exerted a normal coagulation promoting activity on the blood of a known hemophiliac whose coagulation time was greatly prolonged. 2. Normal plasma and the plasma of a person with hemophilia in the same dilutions caused the same reduction of the patient's coagulation time. 3. Intravenous injection of fraction 1 of Cohn (carrier of the antihemophilic factor) did not reduce the patient's coagulation time, whereas transfusion of normal plasma did, e. g., from 5 hours to 22 minutes after an hour. 4. In vitro the antihemophilic factor did not reduce the coagulation time. 5. The fraction active in hemophilia (which can be precipitated) had no effect on the patient's coagulation time, but coagulation was promoted by the supernatant fluid from which the fraction had been precipitated. The patient's condition was not hypoprothrombinemia, because his prothrombin time (Quick) and the prothrombin content were normal. It was not parahemophilia, because the prolonged prothrombin time of normal stored plasma could be reduced to normal by the addition to it of small quantities of his fresh plasma. It was not hypoproconvertinemia, because the determination of proconvertin in his plasma by Owren's method gave a value that was 60% of normal, his prothrombin time was normal, and the addition of a very small quantity of thromboplastin to his blood greatly reduced the coagulation time, which it does not do in hypoproconvertinemia or parahemophilia. These findings indicate that the patient's condition is characterized by a deficiency of a thromboplastin component differing from the one lacking in hemophilia. It now appears that factor 3, previously isolated by the authors from normal thrombocytes, the Christmas factor, and the antihemophilic factor all participate in thromboplastin formation.

1:861-910 (May 2) 1953

Behaviour in Childhood. N. B. Capon.—p. 861.
Amine Oxidase, Pressor Amines, and Cholinesterase in Brain Tumours. E. Bülbring, F. J. Philpot and F. D. Bosanquet.—p. 865.
*Influence of Tolazoline Hydrochloride (Priscol) on Cerebral Blood-Flow in Patients with Mitral Stenosis. H. A. Dewar, S. G. Owen and A. R. Jenkins.—p. 867.
Prognosis and Treatment in Acute Perforated Peptic Ulcer: Review of 206 Cases. J. Gilmour.—p. 870.
*Treatment of Thyrotoxicosis with "Neo Mercazole" (2-Carbethoxythio-1-Methylglyoxaline): Report of 120 Cases. D. Doniach.—p. 873.
Thyrotoxicosis Treated with 2-Carbethoxythio-1-Methylglyoxaline ('Neo Mercazole'). H. Poate.—p. 879.
Anti-Thyroid Activity of 2-Carbethoxythio-1-Methylglyoxaline. A. G. Macgregor and H. Miller.—p. 881.
Cryoglobulinaemia in Alcoholic Cirrhosis. L. L. Griffiths and L. Gilchrist.—p. 882.

Tolazoline and Cerebral Blood Flow.—The cerebral blood flow was estimated by the nitrous oxide method in six patients with mitral stenosis before and after intravenous injections of the vasodilator tolazoline hydrochloride. In the first two patients the cerebral venous blood was sampled through a cardiac catheter, the tip of which had been placed in the left superior jugular bulb under fluoroscopic control. In the remaining four patients, constant rate samples of blood were withdrawn from the superior jugular bulb and a peripheral artery by means of an electrically operated syringe device during inhalation of a nonanesthetic concentration of nitrous oxide for 10 minutes. At least 25 minutes between the first and second estimations were allowed for nitrous oxide desaturation: two to three minutes before the second flow was begun 20 to 30 mg. of tolazoline in 0.8 to 1.2 cc. were injected intravenously. Results showed a striking and significant decrease in

the cerebral vascular resistance after administration of tolazoline, averaging about 25%; and an increase in the mean cerebral blood flow per unit weight of brain tissue of a similar order. These changes suggest that the primary action of tolazoline is vasodilatation, its effect on the cerebral blood flow being a function of its effect on the mean arterial pressure. It therefore seems reasonable to regard the action of tolazoline on the cerebral circulation as essentially histamine-like but differing from that of histamine in that effective cerebral arterial pressure is maintained with consequent increase in mean flow rates. Pending both the results of further investigations along these lines and controlled clinical assessment of the practical value of tolazoline, the authors suggest that the use of tolazoline in the emergency treatment of cerebral embolism in young patients with rheumatic heart disease is justified on theoretical grounds, since augmentation of the cerebral circulation by dilating the vessels and increasing the blood flow through them is clearly the aim of such therapy.

Modified Methimazole (Neomercazole) in Treatment of Thyrotoxicosis. — Neomercazole (2-carbethoxythio-1-methyl-glyoxaline) a modification of methimazole (Tapazole) was given a therapeutic trial in 120 patients with thyrotoxicosis who were followed for periods up to 21 months. Of the 120 patients, 30 received the drug as a preoperative medication and 90 as curative treatment. The optimum initial doses of the drug were 15, 30, and 45 mg. daily for patients with mild, average, and severe thyrotoxicosis respectively. Within two to eight weeks 93 became euthyroid and 27 responded more slowly. Nine of the latter group were operated on and the remaining 18 were controlled in three to six months. Goitrogenic reactions were avoided in all except seven patients by careful control of the maintenance dose, which varied from 4 to 20 mg. daily, keeping the basal metabolic rate between 0 and —10%. No toxic reactions were seen. Comparison of the author's results with those obtained with methimazole by other workers suggest that, weight for weight, neomercazole is at least as effective as, and very much less toxic than methimazole.

Lyon Chirurgical

48:257-384 (April) 1953

*Electroencephalographic Evaluation of Anesthesia During Prolonged Surgical Interventions. P. Santy, J.-C. Sournia and J. Courjon.—p. 257.
Abuse of Neurological Operations Directed Against Pain. R. Leriche.—p. 265.
Clinical Documents for Study of Role of Thyroid Secretion in Development of Cancer. M. Dargent and J. Lavigne.—p. 269.
Transpleural Approach to Renal Area. J. Foret and C. Maquinay.—p. 289.
Operative Risk in Lithiasis of Choledochus: II. Indications Offered for Choice of Technique. P. Mallet-Guy and M. Gangolphe.—p. 301.
Postoperative Recurrences in Solitary Nonparasitic Cysts in Bones. J. Creyssel and P. Barry.—p. 322.

Electroencephalographic Evaluation of Anesthesia During Prolonged Surgical Interventions.—Various factors, such as operative shock, anoxia, and the accumulation of CO_2 in the blood, have been blamed for otherwise unexplained deaths during or immediately after surgical interventions. Although the exact mechanism by which such deaths are caused is not known, the brain is admittedly involved, either primarily or secondarily. Early detection of cerebral changes by encephalography during an operation may make it possible to apply a remedy before the resulting disturbances in bodily function become irreversible. Eleven patients undergoing intrathoracic operations lasting from four to five hours were kept under continuous electroencephalographic observation throughout the procedure. The tracings showed six simultaneous leads, and in every case a preliminary control tracing was made in the waking state. A combination of thiopental, nitrous oxide, and curare was used for anesthesia for all the patients, and the tracings confirmed the clinical impression that the period of induction is especially dangerous. Curare had no effect on cerebral activity, but induction of anesthesia with thiopental sodium, approximately 40 cg., prior to intubation produced profound changes. Large slow delta waves (1 to 2 cycles a second) appeared in all the leads for from 30 to 60 seconds, followed by abrupt extinction of the rhythm; the tracing resembled the picture presented after a generalized epileptic attack, a very severe closed skull injury, or in the moments immediately before death. This phase of complete extinction, which is variable in length, is followed by slow waves (2 to 3 cycles a second) and zones of extinction alternately, each lasting for from 5 to 10 seconds. The disturbed period varies in length from 1½ to 8 minutes. These findings clearly show the dangers accompanying the intravenous injection of barbiturates in large doses, and especially at a rapid rate; when the injection is given slowly, the changes are not the same. Electroencephalographic observation shows any variations that may occur in the depth of the anesthesia as the operation proceeds: deep sleep may be followed by periods in which the tracing is almost the same as that of the waking state. Undesirable variations of this kind seldom occur under skilled anesthetic management, but the absence of clinical signs makes it difficult to judge the efficacy of the anesthesia at all times. Changes in the tracings provide the earliest indication of cerebral distress. The difficult period of awakening is influenced by many factors that complicate the tracings, but signs of cerebral disturbances associated with recovery of consciousness can be detected.

Medical Journal of Australia, Sydney

1:429-464 (March 28) 1953

Study of Medicine Overseas. A. E. Lee.—p. 429.
Some Aspects of Rehabilitation and Placement of Incapacitated Worker. W. E. George.—p. 435.
Rehabilitation and Placement of Incapacitated Worker. G. G. Burniston.—p. 440.
Observations on Biliary Calculus Ulcerating into Small Intestine. L. I. Burt.—p. 444.
Adoption and Fostering of Children. M. Gilchrist.—p. 445.
Cough, Faintness and Syncope. M. Glick.—p. 447.

1:465-496 (April 4) 1953

Present-Day Concepts of Epilepsy. E. G. Robertson.—p. 465.
Structural Basis of Epilepsy. L. B. Cox.—p. 468.
Queer Turns—Lesser Known Manifestations of Epilepsy. J. F. Williams.—p. 469.
Drug Treatment of Epilepsy. G. Selby.—p. 471.
Psychological and Social Management of Epileptic Patient. G. Springthorpe.—p. 474.
Microtechnique for Measuring Haematocrit Value. I. Kaldor.—p. 476.
Murray Valley Encephalitis: Contrasting Epidemiological Picture in 1951 and 1952. S. G. Anderson and M. Eagle.—p. 478.

1:497-532 (April 11) 1953. **Partial Index**

Cancer of Uterus: Wertheim Operation. H. H. Schlink.—p. 503.
Pregnancy and Malignant Disease. R. B. C. Stevenson.—p. 508.
Treatment of Cutaneous Neoplasms. W. C. T. Upton.—p. 512.

Medicina Contemporânea, Lisbon

71:175-292 (April) 1953. **Partial Index**

*Thrombosis of Internal Carotid Artery: Visibility of Vessels of Posterior Fossa. Egas Moniz.—p. 175.
Vectocardiography of Myocardial Infarction. I. Benzecry, D. P. Stein and P. Cozanel.—p. 183.
Experimental Aortography with Cardiac Puncture. A. de Sousa and B. de Morais.—p. 199.

Thrombosis of Internal Carotid Artery.—The angiographic aspect of the blood vessels of the cerebral posterior fossa has not been reported in the literature. The author reports a patient with the complaint of vertigo of nine years' standing. Two years previously he had a stroke that resulted in left-sided hemiplegia. A presumptive diagnosis of thrombosis of the internal carotid artery was made. Angiography was performed by injection of the opaque substance into the right subclavian artery. Three angiograms were made at intervals of two minutes. The first angiogram showed a thrombus lodged at the point of bifurcation of the internal carotid artery. The angiogram was typical for thrombosis of the internal carotid artery with visualized greatly dilated blood vessels, especially of the external carotid artery and its branches. The medium was seen entering the blood vessels of the posterior cerebral fossa, a small portion of the vertebral artery in the cervical region. The basilar, posterior cerebral, and posterior communicating arteries became visible. In the second angiogram the external carotid artery and its branches were no longer visible, whereas the blood vessels of the posterior cerebral fossa showed up

very clearly, being principally the posterior cerebral artery and the cerebellar arteries. In the third angiogram the venous circulation of the posterior cerebral fossa was clearly visible. The mechanism by which blood vessels become visible in the posterior fossa when the opaque substance is injected into the right subclavian artery in thrombosis of the internal carotid artery is complicated. The author believes that in his case the increased blood supply to the right cerebral hemisphere through the enlarged anterior communicating artery was the reason for the improvement in the motor function experienced by the patient in the course of two years.

Minerva Ginecologica, Turin

5:105-160 (Feb. 28) 1953. **Partial Index**

Clinical, Anatomic and Histopathological Study of Uterine Myomas Operated on After Actinotherapy. G. Valle.—p. 107.
Pelvic Endometriosis: Clinical Contribution to Sampson's Pathogenic Theory. G. Garrone.—p. 119.
Influence of Gynecological Laparotomy on Sensitivity of Skin at Site of Incision. M. Uglietti.—p. 131.
*Experiments with Some Antiseptics Proposed for Disinfection of Hands in Obstetrics. G. Massone.—p. 134.

Study of New Hand Disinfectants.—Test experiments are reported of the activity of three antiseptics for disinfection of hands. The new products were hexachlorophene (Gamophen), Desogen, a quaternary ammonium compound, and Dudolo, a fluid disinfectant consisting of an organic mercury compound to which *p*-chloro-*m*-cresol and *p*-chloroxylenol are added. A five minute scrubbing with the new soap and warm water had more effect than the usual 10 minute scrubbing with soap and warm water followed by a five minute disinfection in a solution containing 70% alcohol. With a 5% solution of Desogen the washing time was reduced to eight minutes of which the first three were used for scrubbing with soap and warm water. With Dudolo in a 1:1 solution the washing time was reduced to six minutes and in this case also the first three minutes were used for scrubbing with soap and warm water. Not only was the washing time shortened with the new products but their antiseptic action was more pronounced and lasted longer. When pilocarpine was used to stimulate sweating, the increase of the bacterial flora on the skin of the hands was much greater in persons who had used the common washing procedure. The most revealing data were obtained in another experiment. It is known that after lengthy operations microscopic defects are present in the surgeon's gloves and that bacteria can pass through them. Some persons wore gloves after washing their hands with the usual method and others after using the new products. They were then made to manipulate sterile material. One-half hour later a few bacterial colonies could already be discovered on the hands of the persons of the first group, and after two hours the number of these colonies had increased considerably. The number of colonies that appeared in the same period of time on the hands of the persons of the second group was much smaller. The positive features of the products were thus proved, although the author could not determine whether they were due to bactericidal or to bacteriostatic action. Except for Dudolo, these antiseptics must be used daily to obtain good results, but this does not contraindicate their use. In addition to their low cost and pleasant odor, these products do not have any toxic effect on the tissues.

Minerva Medica, Turin

44:607-644 (March 10) 1953. **Partial Index**

Truncus Arteriosus a Rare Type of Congenital Heart Disease: Clinical, Angiocardiographic and Hemodynamic Study of Four Cases. P. F. Angelino and A. Actis-Dato.—p. 613.
*Prophylaxis of Postoperative Vomiting in Patients After General Anesthesia. O. Colombo and G. Calligari.—p. 625.
Myasthenia and Pseudomyasthenia Reactions. A. Salmon.—p. 629.

Prophylaxis of Postoperative Vomiting.—The authors review the literature on the center of origin of postoperative vomiting and report results of a study made on 502 patients in whom surgery was performed under general anesthesia mainly for gynecological lesions. They divided the patients into three groups according to the premedication. The first group consisted of 65 patients in whom premedication was not practiced. The second group comprised 179 patients who were given alkalinizing agents during the day preceding the operation and 1 tablet of phenobarbital and 1 or 2 tablets of histamine-antagonizing agents in the evening. The third group of 258 patients received, in addition to the drugs given to the second group, one or two vials of Cortigen B_8 (each vial contained 12 units of an extract of total adrenal cortex in which epinephrine was not present and 50 mg. of pyridoxine). Glucose and ascorbic acid were also given to some patients of this group. There was vomiting in 16 patients of the first group (24%), 22 of the second (12.5%), and only 14 of the third (6%). There was nausea in 7.7%, 4%, and 3%, respectively. Although the alkalinizing and histamine-antagonizing agents were beneficial in preventing vomiting, better results were obtained when Cortigen B_8 was added.

44:927-958 (April 11) 1953. **Partial Index**

Low-Grade Fevers. P. Bastiai.—p. 927.
Fever Therapy. E. Antoniazzi.—p. 929.
Clinics and Therapy of Pulmonary Insufficiency. G. Giordano.—p. 936.
*Possible Therapy of Undulant Fever with Oral Administration of Small Doses of Aureomycin and Intradermal Administration of Vaccine. M. Poli.—p. 946.

Aureomycin and Vaccine Therapy in Undulant Fever.—A 42-year-old man, who had had a low-grade fever for 47 days, complained of chills in the evening, pain in the right hypochondrium and muscles of the legs, anorexia, asthenia, headache, and night sweats. On hospitalization his serum was positive for Brucella melitensis. He was given orally 0.25 gm. of aureomycin daily in divided doses every six hours and intradermally polyvalent vaccine containing 10 million bacteria. This therapy was continued for 15 days, after which the vaccine was given alone for three more days. At the same time the patient received orally 0.50 gm. of chloramphenicol (Chloromycetin) daily for five days. This was given to alleviate a pain in the gallbladder area, since Escherichia coli had been recovered from the duodenum. The pain disappeared by the third day and the temperature had returned to normal by the fourth. A low-grade temperature reappeared nine days after the antibiotic therapy was discontinued. A second course of aureomycin was begun and continued for nine days. On the second day the temperature was again normal. A total of 6 gm. of aureomycin was given during the two courses. There were no untoward effects, although each injection of vaccine was followed by an intense local reaction with formation of a large papule. The erythrocyte sedimentation rate decreased rapidly, and the agglutination titer that at the time of hospitalization was 1:2,000 had become 1:4,000 on the fifth day and 1:8,000 on the 11th day. Thus while the antibiotic exerted a bacteriostatic action on the Br. melitensis organisms by arresting their development, the vaccine increased the antibody titer and thus enabled the organism to participate actively in the fight against the infection. Three months later the patient was in excellent general condition and had gained 10 kg. in weight. He complained of a pain in the gallbladder area and was given chloramphenicol orally.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

97:861-920 (April 4) 1953. **Partial Index**

Disturbances in Circulation of Cerebrospinal Fluid and Their Treatment. A. van der Zwan.—p. 865.
Hypervitaminosis A. H. J. Klein Obbink and C. Nieman.—p. 872.
*DDT Intoxication in an Infant. D. P. R. Keizer.—p. 882.
Value of Prophylactic Vaccination Against Diphtheria. A. L. Noordam.—p. 886.

DDT Intoxication in an Infant.—An infant born in a maternity hospital was placed in a bed in its home with bed clothing that had been heavily powdered with a material containing chlorophenothane (DDT) and pyrethrum. Anorexia, vomiting, diarrhea, muscular spasm, tremor, and mild renal and hepatic changes appeared. Chlorophenothane poisoning was considered the cause of the symptoms. Later, subcutaneous fat induration developed in the extremities and were diagnosed as subcutaneous neonatal adiponecrosis. Since these indurations could not be traced to trauma, it is assumed that these also were caused by chlorophenothane intoxication. After a period of hospitalization, the child was sufficiently improved to be discharged.

Nordisk Medicin, Stockholm

49:527-560 (April 10) 1953. **Partial Index**

*Diabetes Mellitus and Pregnancy. G. Svanteson.—p. 533.
Endometrial Biopsies in Women Treated with ACTH. E. Secher.—p. 536.
Preinvasive Cervical Cancer: Diagnosis and Treatment. H. Arfwedson and S. Winblad.—p. 537.
Cancer of Uterus and Ovaries with Special Regard to Symptomatology. L. Hagbard.—p. 540.
Urinary Incontinence. P. Westerberg.—p. 542.
Cystometric Method with Continuous Recording. S. Englund.—p. 544.
Neonatal Care of Infants of Diabetic Mothers. S. Joachimsson.—p. 546.

Diabetes Mellitus and Pregnancy.—Svanteson reports 15 cases of pregnancy with diabetes in 14 women. His principle of treatment is close control of the patient's diabetes and pregnancy, prophylactic cesarean section in the 36th week, and immediate transfer of the infant to the children's department of the hospital. Eleven mothers were delivered by cesarean section, one of them twice; three were delivered spontaneously, one with hydramnios and stillborn fetus in the 31st week, one with hydramnios in the 35th week, and one in the 36th week on admission for cesarean section. All the mothers survived. In two cases there was slight albuminuria and in one case marked retinopathy that disappeared during the pregnancy. The infants were without deformities.

Philippine Medical Association Journal, Manila

29:105-148 (March) 1953

Prenatal Syphilis. J. O. Quiason and L. M. Ibarra.—p. 105.
Imperforate Anus with Recto-Urethral Fistula (Report of Case of Five-Day Old Boy). G. F. Gadi and E. B. Gadi.—p. 114.
Challenge of Iatrogenic Disease. R. V. Guiang.—p. 116.
Efficacy of Anti-Smallpox Vaccination by Intradermal Method: (Preliminary Report). N. Victoriano.—p. 120.

Presse Médicale, Paris

61:503-520 (April 4) 1953

*Prophylaxis and Therapy of Phlebitis with Heparin Given Intradermally. C. Olivier.—p. 503.
Gout with Rheumatic Symptomatology. J. Sérane.—p. 504.

Intradermal Administration of Heparin in Phlebitis.—According to Olivier, intravenous administration of heparin combined with oral administration of coumarin derivatives is the method of choice in the treatment of hospitalized patients with recent thrombosis of the deep veins. In certain patients who have recently been subjected to operations for venous thrombosis repeated injections of heparin into the subcutaneous network may prove undesirable. In patients treated at home at a considerable distance from large centers, only heparin may be employed because it does not require control determinations. This therapy frequently has to be discontinued before the patients have resumed walking because of painful reactions and the occurrence of hematoma at the site of the injection following repeated intravenous injections of heparin. The author treated 15 patients with thrombosis of the deep veins or with pulmonary embolism by injecting heparin into the healthy skin in an area not involved by edema, usually into the external aspect of the shoulder. The dose commonly used was 200 mg. in the morning and in the evening, i. e., 1 cc. of a pure 20% solution standardized at 100 I. U. per milligram without the addition of procaine hydrochloride or of a diffusion factor. The intradermal injections did not cause pain or hematoma at the site of the injection. Clotting time tests were carried out according to Lee and White's three tube technique. The test made before the first injection revealed in general that the clotting time was a few minutes less than normal. From the fourth to the eighth hour the clotting time was more than double the normal. This occurred regularly only on the second day of the treatment, suggesting that intradermal heparin therapy should be considered only for maintenance treatment. The thromboembolic disease did not become worse, and there was no recurrence. Hemorrhagic side-effects consisted of a spontaneous hematoma of the lower third of the rectus abdominis muscle in one patient on the 16th day after gastrectomy and five days after the dose of the heparin had been increased to 400 mg. twice a day, and of a parietal hematoma in an emaciated patient on the third day of treatment with doses of 200 mg. of heparin twice a day for pulmonary infarction. In the first patient the clotting time had been increased from 15 to 61 minutes and in the second from 12 to 65 minutes. A dose of 200 mg. twice a day may be employed in patients whose body weight exceeds 132 lb. (60 kg.), but caution is indicated in emaciated patients and on the day following an embolism.

61:627-644 (May 2) 1953. **Partial Index**

*Genuine Antibiotic Aerosols and Pulmonary Tuberculosis. J. Paraf, P. Zivy, M. Paraf and others.—p. 627.
Physiological Bases of Therapeutic Action of Ultrasonic Waves. P. Chauchard, H. Mazoué, R.-G. Busnel and J. Gligorijevic.—p. 628.
Congenital Renal Malformations in Children. J.-F. Porge.—p. 629.

Antibiotic Aerosols and Pulmonary Tuberculosis.—The concentration of antibiotics in the blood must not only be supplemented by concentrations in the tissues and the lesions if tuberculosis is to be treated successfully but must also be maintained at effective levels for substantial periods. Genuine, or stable, aerosols introduced into cavities and diseased bronchi should produce the favorable conditions obtained by surgical treatment, that is, bronchial disinfection and drainage combined with massive application of antibiotics to the cavity walls. Most of the efforts hitherto made in this direction have been only moderately successful, probably because the antibiotic was rapidly eliminated. The rapid declines in concentration noted in some reports could not have occurred if a truly stable aerosol with negatively charged particles of from 0.5 to 2 μ in size had been used. The authors found that *p*-aminosalicylic acid incorporated in an aerosol meeting these requirements did not appear in the blood until from three to six hours after aerosolization. It quickly attained a maximum level and then declined very slowly, showing that prolonged contact between the antibiotic and the tissues had been secured. Tests proved that the concentration of the antibiotic in the blood was greater than that obtained by oral administration and that it remained at a therapeutic level for a long period. Aerosol treatment properly used in combination with general antibiotic therapy may be expected to increase the percentage of antibiotic cures in pulmonary tuberculosis.

61:645-660 (May 6) 1953. **Partial Index**

*Preliminary Results of First Center of Systematic Detection of Tumors of the Gastrointestinal Tract, Based on a System of Clinical Predetection by Echelon. G. Albot, M. Parturier-Albot, N. Bernard and others.—p. 645.
Granular-Cell Pseudotumor and Spino-Cellular Epithelioma of Arytenoid Cartilage; Cervical Metatasis of the Epithelioma. J. F. Martin, M. Dargent and J. Feroldi.—p. 648.
*Prolonged Sleep Treatment in Psychiatry. J. Bastié and A. Fernandez.—p. 651.

Systematic Detection of Tumors of Gastrointestinal Tract.—According to Albot and co-workers, systematic mass detection of tumors of the gastrointestinal tract has been practiced successfully for several years at the regional office of the Social Security Fund in Paris. To be economic and to yield significant results, systematic detection of the tumors depends on clinical predetection in stages. Selection of patients by systematic examination of all healthy persons with the aid of fluoroscopy, gastric intubation, rectoscope, and blood tests does not seem to be practicable. On the contrary, preliminary clinical detection by various medical teams has proved effective. The first selection is done by the roentgenologic examination of patients with dyspepsia or mild anorectal or intestinal disturbances who might have cancer; it is done by assistant social workers. The second phase of clinical detection is carried out by controller-physicians of social insurance funds, by plant physicians, and by the physicians of centers for systematic health examinations. It consists of eliminating from patients with minor disturbances suspected of having malignant lesions those whose condition is definitely benign, and sending those whose condition cannot be definitely ascertained to the detection center for tumors of the gastrointestinal tract. There, the third phase of clinical detection takes place. It is carried out by a team of specialists grouped around one or several experts at this center. It is on this "concentrated" group of patients that the technical and financial efforts of the detection center should be expended. Statistical data from 1946 to 1952 revealed that by this method the ratio of detected cancers as compared to the number of

patients examined became much higher than with other methods of mass detection. Cancer was detected in 57 of 2,799 patients examined at the detection center for gastrointestinal tumors. Of these 57, 23 had cancer of the stomach, 23 cancer of the rectum, anus, sigmoid or cecum, 9 cancer of the esophagus and cardia, 1 cancer of the liver, and 1 cancer of the pancreas. This is a ratio of 20.3 per thousand, or one case of cancer detected among 50 patients examined, as compared to a ratio of 1 to 3 per thousand detected with other methods. Of 1,329 patients with anorectal disturbance who had a systematic rectoscopic examination, cancer of the rectum was detected in 18, i. e., a ratio of 13.5 per thousand. Seventeen of the 18 patients presented a long course that had not been recognized. Organizing procedures such as those reported by the authors are easy if full advantage is taken of all controls already exerted by social insurance, industrial medicine, and public health examinations. Combined with the findings from the detection center, they should be made available to all practitioners.

Prolonged Sleep in Psychiatric Treatment.—On the basis of Pavlov's concept of the internal inhibition of conditioned reflexes by sleep, the authors treated 10 women with various mental disorders by interrupted prolonged sleep. For the eight days preceding the sleep treatment the patients were given hepatic extracts, vitamins B_1, C, and P, sympathicotonic drugs, and psychotherapy. The patients were subjected to various examinations concerning the heart, the liver, and the kidneys. Treatment by sleep was instituted on the ninth day. Sleep was induced by hypnotics that affect the cerebral cortex, such as sodium bromide, chloralose, and morphine hydrochloride combined with scopolamine hydrobromide; the diencephalon, such as phenobarbital, aprobarbital diethylamine combined with barbital diethylamine, hexobarbital sodium, thiopental sodium; and the autonomous nervous system, such as Phenergan (10-[2-dimethylaminoisopropyl]-phenothiazine), diethazine (Diparcol) hydrochloride, and atropine. There is no uniform dosage scheme for the hypnotics. The dose depends on the type of the nervous system of the patient, his body weight, the nature of the psychopathic process, and the response to the treatment. The hypnotics were administered parenterally and orally five or six times daily at definite and regular hours. Hexobarbital sodium in doses of 0.50 to 1 gm. orally and thiopental sodium in doses of 0.50 to 1 gm. intravenously were used as "sleep starters." An average of 18 to 20 hours per 24 hours of deep or light but always reversible sleep, resembling physiological sleep, was maintained from 25 to 30 days. Only minor physiological changes were observed in the patients; sudden rises in temperature followed by sudden remission occurred once or twice in the course of the treatment; there were also alterations in the arterial blood pressure with a significant drop in the diastolic pressure in two patients with previous hypertension. Of the 10 patients, 4 (those with agitated remittent melancholia, obsessional neurosis, subacute ethylism, and psychic epilepsy) made a complete recovery, while the other 6 were temporarily cured or considerably improved. Protective inhibition of reflexes by sleep may be induced without great risk. It provides the cortex with prolonged rest that makes possible establishment of new regulating mechanisms for the subcortical-cortical connections and better restoration of the balance of the exhausted organism.

Revista Clínica Española, Madrid

48:213-280 (Feb. 28) 1953. **Partial Index**

Syndrome of General Adaptation and Infections. E. Romero.—p. 213.
Differential Diagnosis of Syndromes of Painful Shoulder. J. V. Anastasio. —p. 224.
*Insulin Therapy in Multiple Sclerosis. B. Rodríguez-Arias.—p. 228.
Radiology of Lung After Operation. S. Di Rienzo.—p. 232.

Insulin Therapy in Multiple Sclerosis.—Six patients with typical multiple sclerosis were given insulin subshocks. The insulin injection was given in the morning before breakfast, with an initial dose of from 5 to 15 units of insulin. This was increased daily by 5 or 10 units to a maximal dose of 40 to 60 units or rarely 80 units. The injections were given daily or every other day, with rests on Sundays, up to 15 or 25 injections. The subshock was allowed to last for 1 to 3 hours without reaching the precoma or coma phase. The subshock was discontinued at the end of 3 hours by giving the patient sugar, tea with 100 gm. of sugar, alone or with an intravenous injection of from 10 to 30 cc. of a 40 or 50% hypertonic dextrose solution. Relapsing subshock symptoms were likewise controlled by administration of sugar in an orange-flavored drink, food, and sweets. These doses of insulin produced neurosympathetic symptoms that did not approach precoma or coma phases. The treatment was well tolerated, without accidents or complications. In two cases the treatment was repeated several months after the first for consolidation of good results. In all cases the appetite, nutrition, and general condition of the patients improved. Pain, paresthesia, spasticity, and ataxia were greatly diminished. The patients reported a sense of well-being, which lasted for several months. The treatment is symptomatic. Its palliative or curative effects seem to be due to the stimulating action of insulin on the hepatic functions and on the protection of myelin.

Revista Española de Pediatría, Zaragoza

9:1-164 (Jan.-Feb.) 1953. **Partial Index**

Utility of Tests of Sensitivity to Antibiotics. M. Lust, J. L. Comin, G. Nigrin and Mme. Creteur.—p. 1.
Equations of Growth. J. Teijeira.—p. 25.
Exclusively Serologic Diagnosis of Infantile Visceral Leishmaniosis. R. Marco Ahuir and J. Selfa.—p. 55.
*Rubeolic Embryopathy: Report of Two Cases. E. Miralbell-Andreu. —p. 135.

Congenital Defects Due to Rubella.—Two cases of congenital defects due to rubella are reported. Both infants were born to normal couples who had no familial history of malformations or of congenital cataract. The mother of the first infant had rubella in the first two weeks of her first pregnancy. The infant was seen at the age of 2½ months, and a diagnosis of unilateral congenital cataract of the central type was made. The infant was otherwise normal and had normal hearing. The mother of the second infant had the rubella in the sixth week of her third pregnancy. Her other two children are normal. The infant was seen at the age of 3 days. A diagnosis of bilateral congenital cataract of the central type and of congenital heart disease was made. The nature of the infant's heart disease has not been determined. His hearing is normal. The author advises that gamma globulin be given to a woman who is exposed to rubella in the first trimester of pregnancy. The prophylactic action of the drug lasts 30 days. If any further contact occurs after 30 days, the treatment should be repeated. Induced or natural rubella immunization is not effective.

Revue Neurologique, Paris

88:1-80 (No. 1) 1953

Electromyographic Diagnosis of Myasthenia. F. Thiebaut, F. Isch, and C. Isch-Treussard.—p. 3.
*Epilepsy Caused by Cerebral Tumors (Based on 170 Cases of Epileptogenic Tumors). J.-E. Paillas, J. Bonnal and J. Corriol.—p. 18.

Epilepsy Caused by Cerebral Tumors.—Analysis of 170 cases of epileptogenic tumors showed that epileptic symptoms were most frequent between the ages of 31 and 50 (58%). Epileptic seizures in a child believed to have a cerebral tumor suggest that it is supratentorial, because tumors of the posterior fossa, though frequent in early childhood, rarely cause epilepsy. Epilepsy in an adult is most likely to be neoplastic in origin when it appears after the age of 31. Temporal and frontal tumors account for 60% of the cases of epilepsy in this series; next most frequent as a cause of epilepsy are median and paramedian tumors of the convexity of the hemispheres. The incidence of epilepsy is proportional to the benignity of the tumor; 92 of the tumors causing epilepsy were benign. Generalized grand mal seizures occurred in 66 cases, and were the first symptom of the tumor in 46 patients. Temporal epilepsy, which had the highest incidence (41%), was also often the first sign of a tumor. A true jacksonian seizure or a localized clonus, though the first epileptic manifestation in 31 cases, was the first sign of the tumor in only 21. The

value of the various types of seizure in localizing the tumor is limited, because the focus functionally responsible may be distant from the tumor site. Electroencephalographic study showed irritative waves indicative of epilepsy in only 25% of the cases of malignant tumors and only 37.6% of the cases of benign tumors. Epileptic seizures may recur after surgical removal of a cerebral tumor either because the character of the tumor made complete removal impossible or because faulty technique resulted in formation of excessive scar tissue.

Riforma Medica, Naples

67:457-484 (April 25) 1953. **Partial Index**

*Correlations and Reciprocal Influence of Epinephrine and Nor-Epinephrine on Physiopathology of Circulation: Observations on Man. S. Bardelli and R. Monfardini.—p. 467.

Cystic Emphysema in Bronchopulmonary Neoplasms. R. Miceli.—p. 470.

Effect of Arterenol and Epinephrine on Physiopathology of Cardiovascular Apparatus.—Arterenol diluted in 50 cc. of isotonic sodium chloride solution was given intravenously to 10 patients with no cardiovascular abnormalities in doses of 0.1 mcg. per kilogram of body weight per minute for 20 minutes. Five other patients in the same cardiovascular state received the drug intramuscularly in doses of 0.30 mg. An increase in both systolic and diastolic blood pressures followed in all the patients, and there was also pronounced bradycardia. The drug was well tolerated; the only complaint was a slight headache and constriction in the neck, which became more or less swollen. Two days later the same 10 patients were given intravenously a mixture consisting of equal doses of epinephrine and arterenol. The other five patients received a mixture of equal doses of the two drugs intramuscularly. The systolic and diastolic pressures increased to a lesser degree than when arterenol had been given alone; in some instances the values remained unchanged. There was also a lesser degree of bradycardia. Side-effects, when present, were much milder. The vasomotor action of arterenol was thus decreased by that of epinephrine. This seems to prove the hypothesis advanced by Goldenberg that there is in the human organism a hemodynamic equilibrium that is governed by a ratio between these two substances that are in some respects antagonists. An alteration of this ratio because of epinephrine deficiency leads to vasospasm and thereafter to hypertension.

Schweizerische medizinische Wochenschrift, Basel

83:349-372 (April 11) 1953. **Partial Index**

Alkalotic and Acidotic Hypopotassemia as Cause and Sequela of Functional Disturbances of Kidney. A. Labhart and O. Spühler.—p. 349.

Treatment of Hemophilic Hematoma and Hemarthrosis with Short Wave Irradiation. A. Fonio.—p. 253.

Attempt at Diagnosis and Treatment of Atypical Pneumonia Caused by the Parasite Pneumocystis Carinii in Suckling Infants: Preliminary Report. J. Dvorák.—p. 354.

*Lysergic Acid Ethylamide, a New Antipsychotic Drug with Strong Sedative Effect, Obtained from Ergot; Preliminary Report. H. Solms.—p. 356.

Lysergic Acid Ethylamide, a New Antipsychotic Drug.—Twenty-seven subcutaneous injections of lysergic acid ethylamide, a half-synthetic ergot alkaloid, were given to eight normal men. The dose varied from 0.25 mg. to 0.2 mg.; the average amount administered was 0.5 to 0.75 mg. Two distinct phases of the effect of the drug could be distinguished. The first phase of 15 minutes duration was characterized by benign neurovegetative irritative and sensomotor symptoms and by mild discomfort such as occasional salivation, secretion of tears, sweating, ataxia, hyperreflexia, and paresthesia. There was occasional nausea, heavy breathing, and sensation of vibration and tension in the muscles. The second phase of one and a half hour duration was one of psychosis, with a sudden onset of personality changes and simultaneous disappearance of discomfort. The psychopathological aspect was that of a schizophrenia-like condition of asthenia, indifference, and disturbance of volition, with intensive phenomena of depersonalization without sleep. A mild hallucinosis syndrome resulted on nine occasions from injections with higher doses, and in five instances it was associated with exaggerated impulses, decreased inhibition, and unmotivated laughing. The after effect of a single injection of lysergic acid ethylamide consisted of deep night sleep, occasional fatigue, and mild weakness of concentration and memory. Twenty chronic patients with schizophrenia and oligophrenia were given 402 applications of lysergic acid ethylamide, either 0.25 to 1 mg. subcutaneously or 0.5 to 1.5 mg. (one to three tablets) by mouth three times daily. Sedation of paranoid-hallucinatory excitation resulted for one to four hours; hallucinations did not subside but became milder. The patients became apathetic and more indifferent to their illusions. Several patients received 0.25 to 0.5 mg. subcutaneously daily for two weeks and six weeks, respectively, as a continued sedative during the day, with the result that perception was retained but apperception was abolished. Occasionally patients with acute catatonia who had become accustomed to high doses of morphine-scopolamine and barbiturates reacted promptly and favorably to doses of 0.5 to 1 mg. of lysergic acid ethylamide, but in general lysergic acid ethylamide was not sufficient in severe excitation, and the limit of tolerance was usually reached by increasing the dose from 1 to 2 mg. Lysergic acid ethylamide proved to be an effective soporific, inducing sleep for three to five hours in patients with schizophrenia and oligophrenia who were suffering from long-continued disturbances of sleep or mild restlessness during the night. The effect of 0.3 to 0.5 mg. of lysergic acid ethylamide subcutaneously or of 2 tablets of 0.5 mg. orally equaled that of 1 to 3 gm. chloral, 0.8 gm. of sulfonmethane, or 0.5 to 1 gm. of barbital sodium. The effect of the lysergic acid ethylamide on the paranoid-hallucinatory condition of excitation in schizophrenic patients is that of a reversible "chemical lobotomy." The drug is a new type of sedative that belongs neither to the hypnotics or narcotics of barbituric acid or morphine type nor to the sympathicolytics or parasympathicolytics with a predominantly blocking effect on the autonomic nervous system.

Semaine des Hôpitaux de Paris

29:1329-1394 (April 26) 1953. **Partial Index**

White Pneumonia. R. Lutembacher.—p. 1329.

Bacteriotherapy is Still Useful. M. Larget and J.-P. Lamare.—p. 1331.

*Acute Thrombopenic Purpura with Autoagglutination (Demonstration in vitro of an Antiplatelet Agglutinin). J. Dausset, P. Delafontaine, G. Damiens and Y. Fleuriot.—p. 1334.

Treatment of Cardiac Edema by Schemm's Method. A. Abaza and A. Akriche.—p. 1339.

Unilateral Polycystic Kidney. J. E. Marcel.—p. 1351.

Acute Thrombopenic Purpura with Autoagglutination.—Serologic study of the blood of a woman, aged 30, with acute thrombopenic purpura showed previously unreported phenomena of agglutination and destruction in vitro of normal platelets and inhibition of normal clot retraction. Her illness began on Dec. 14, 1951, with general feverish malaise, followed a week later by petechiae on the backs of the hands and slight gingival bleeding. The purpuric manifestations increased and the temperature, which had returned to nearly normal levels, rose again to 39 or 40 C. Pallor indicated the rapid development of intense anemia. No source of infection was found, and careful study of the patient's history failed to show foreign toxins of any kind; in particular, there was no habitual use of hypnotics. The only factor of interest was a subfebrile episode with monocytosis and pronounced acceleration of the erythrocyte sedimentation rate some months earlier. The impossibility of determining the etiology of this purpura with anemia led to the institution of treatment with antibiotics and whole blood transfusions, but the patient's condition deteriorated and she died on Jan. 11, 1952. Autopsy was not permitted. Addition of the patient's serum to suspensions of normal platelets in their own citrated or heparinized plasma resulted in their rapid agglutination and destruction. Clot retraction was completely inhibited when the serum was added in equal parts to whole blood or citrated and recalcified plasma. This inhibitory action, however, took place only when calcium was present. A diagnosis of immunologic thrombopenic purpura with autoagglutination was strongly indicated, but could not be confirmed.

Strahlentherapie, Munich

90:325-484 (No. 3) 1953. Partial Index

Effects of Light in Their Pharmacologic and Physiological Relationships. P. Wels.—p. 325.
Effect of Roentgen Rays and of Cancerogenous Substance "Styryl" on Embryonal Development. H. R. Schinz and H. Fritz-Niggli.—p. 345.
Biophysical Viewpoints in Medical Research on Isotopes. B. Rajewsky and O. Hug.—p. 361.
Methods for Performance of Tests Controlling the Protection Against Roentgen and Gamma Rays, Using New Devices. B. Rajewski and R. Jaeger.—p. 373.
*Value of Blood Picture as Indicator of Damage Caused by Irradiation. H. Langendorff.—p. 408.
*Comparison of Effects of Roentgen and Radium Irradiation on Human Skin. F. Wachsmann.—p. 438.

Blood Picture as Indicator of Irradiation Damage.—In an attempt to determine the tolerance of the organism to irradiation with the aid of blood studies, 30 rats were given irradiation treatment with 2.5 r daily for one year. The other technical factors were 92 kv., 10 ma, 0.5 mm. aluminum filtration, focal-skin distance 80 cm., and daily irradiation time of 13 seconds. Eight of the 30 animals died, 6 of these between the 44th and 52nd week. The white blood cells, particularly the lymphocytes, were studied in 1,574 blood smears. The blood for the differential blood count was withdrawn from the vein of the tail at weekly intervals. The spleen and the testes removed from the animals who died spontaneously and from others who were killed when in a dying state were examined microscopically. Weekly counts of the leukocytes and particularly of the lymphocytes did not show any changes that might have indicated damage due to irradiation. As contrasted with these observations, the histological appearance of the tissues from the testes and spleen showed that these organs had been moderately damaged. Many of the seminal tubules of the testes did not contain any spermatozoa, while spermatoblasts were frequently present in large numbers. Spermatogonia were also present in large numbers. The changes in the spleen consisted of a reduction of the lymphatic tissue, deficiency of some of the germinal centers, and some increase of the erythropoietic tissue. There is evidence that this irradiation damage may be compensated intensively by the regenerative capacity of the blood-forming tissue, the testes and the spleen and that Jacobson's protective humoral factor may be considered significant with respect to the spleen and the hematopoietic system. As a result of his experience, the author states that the blood picture has only limited value as an indicator of irradiation damage after the application of small doses of irradiation for long periods.

Effects of Roentgen and Radium Irradiation on Human Skin.—An attempt was made to compare the effects of roentgen irradiation with that of radium-gamma irradiation. The skin of the thigh of patients with carcinoma and the skin of pigs were exposed to roentgen rays using a tension of 45 to 200 kv., and to radium-gamma rays under such conditions that distribution of the dose with respect to space and time was equal as much as possible, i. e., the size of the field, the relative depth dose and the dose rate were all equal. The "built-up effect" on which an increase of the depth dose of the ultra-hard rays depends was excluded by interposed tissue-equivalent filters made with Trolitul (a type of varnish). Equal doses thus were applied to the irradiated skin. Results showed that in order to produce the same erythematous reaction of medium degree twice as much radium-gamma irradiation dose is required as roentgen ray irradiation. Furthermore it was demonstrated that the "dose-equivalent" of the radium-gamma irradiation depends on the dose, i. e., that with small doses (erythema threshold) approximately three times as much gamma irradiation, and with large doses (epitheliolysis up to necrosis) approximately two to one and half times as much gamma irradiation has to be applied in order to elicit the same skin reaction as with roentgen irradiation using a tension of 45 to 200 kv. It is emphasized that this lesser effect of the radium-gamma irradiation applies only to the human skin and the skin of pigs; it may be explained only by the specific ionization density of roentgen and radium-gamma irradiation.

Tubercle, London

34:99-126 (April) 1953

Concentration of PAS in Blood During Medication with PAS or PAS-Salts. H. Nilsson.—p. 100.
Provisional Law Describing Conditions for Perpetuation of Tuberculous Infection and Principles of Contact; Appendix on Some Applications of Foregoing to Tuberculosis Control Policy. F. A. Nash.—p. 105.
Tuberculin Testing in Day Nurseries. J. T. N. Roe.—p. 110.
*Hypokalaemia with Hypotension Due to PAS Therapy. G. P. Jones and P. O. Leggat.—p. 112.

Hypopotassemia with Hypertension Due to *p*-Aminosalicylic Acid.—The occurrence of hypopotassemia in association with cardiovascular hypotension in a 60-year-old man with chronic bilateral fibrocaseous tuberculosis who had received 27 gm. of streptomycin and 1,008 gm. of sodium *p*-aminosalicylic acid is reported. Following two days of severe vomiting and diarrhea, muscle weakness developed gradually. He was afebrile, with a pulse rate of 70 to 80 per minute. Blood pressure was 140/80. No abnormal murmurs or changes in heart sounds were detected, but an occasional premature beat was heard. The serum potassium level was 10 mg. per 100 cc. The electrocardiogram showed a Q-T interval of 0.5 second. The cerebrospinal fluid pressure was normal, the potassium content of the cerebrospinal fluid being 12 mg. per 100 cc. Since the patient could tolerate a full diet, no additional potassium therapy was given. Serial serum potassium estimations showed a gradual rise and in two days power was obviously returning to the paretic muscles. Two weeks after admission to the hospital full power was present in the trunk and limbs. The blood pressure was 210/110 mm. Hg, the serum potassium level was 20 mg., and the electrocardiographic recordings were normal. It is suggested that the low serum potassium was due to diarrhea and vomiting, the frequent accompaniments of treatment with *p*-aminosalicylic acid, and that the hypotension resulted from the primary myocardial effect of the low-serum potassium. Since many patients are treated at their homes with *p*-aminosalicylic acid, often without close supervision, particular attention should be paid to this toxic complication.

Tuberkulosearzt, Stuttgart

7:187-256 (April) 1953. Partial Index

Silicosis and Silico-Tuberculosis. G. Worth.—p. 187.
Formation of Fistulas in the Bronchial Tree. A. Huzly.—p. 194.
Clinical and Bacterial Resistance in the Course of Treatment of Tuberculosis with the New Drugs: Streptomycin, *p*-Aminosalicylic Acid, Amithiozone (TBI), and Isoniazid. E. Dissmann.—p. 205.
Studies on Resistance Against Isoniazid and Its Effect on Tubercle Bacilli Resistant to Streptomycin. T. I. Gökce, H. Özerengin, T. Ciragöz and A. Öztürk.—p. 214.
Isoniazid in Treatment of Pulmonary Tuberculosis. F. Barth.—p. 215.
*Glycosuria and Hyperglycemia Following Treatment with *p*-Aminosalicylic Acid. G. Robel.—p. 224.
*Frequency of Concurrence of Diabetes and Tuberculosis. W. Siedhoff.—p. 225.
Follow-Up Examination of Persons Vaccinated with BCG. G. Jess.—p. 230.
Value of Mass Roentgenoscopy in the Detection of Pulmonary Cancer. J. W. Guiss.—p. 235.

Glycosuria and Hyperglycemia Following Treatment with *p*-Aminosalicylic Acid.—Robel observed elevation of the blood sugar curve in a number of patients who were treated with *p*-aminosalicylic acid. In most cases the hyperglycemia was reversible, but in one case he noticed a more pronounced glycosuria following *p*-aminosalicylic acid therapy and found that after administration of the drug was discontinued and even after glycosuria subsided the fasting blood sugar curve was persistently elevated despite a diabetic diet. The patient died 11 months after cessation of treatment with *p*-aminosalicylic acid, and the hyperglycemia persisted until death, the average fasting blood sugar value being 180 mg. per 100 cc. The history of the patient suggests that prolonged administration of *p*-aminosalicylic acid is capable of producing irreversible changes in the insular apparatus of the pancreas and that it is advisable that fasting blood sugar determinations be made in addition to the usual tests performed during prolonged treatment with this drug, such as differential blood cell counts, determination of hemoglobin

value, and urinalysis. Ambulatory treatment with *p*-aminosalicylic acid is inadvisable in view of the possibility of the development of complications. The reported case recalls similar cases reported by Tempini and Franke in which prolonged administration of *p*-aminosalicylic acid resulted in permanent injury to the insular apparatus of the pancreas.

Frequency of Concurrence of Diabetes Mellitus and Tuberculosis.—In the course of roentgenologic examination of 2,962 patients with diabetes mellitus, Siedhoff discovered that 7.6% had pulmonary tuberculosis. Reports in the literature indicate that the incidence of tuberculosis in diabetic patients varies from 2 to 8.4%. The two diseases concur more frequently in men than in women. The 2,962 diabetic patients observed by the author included 1,158 men, of whom 12.2% had tuberculosis, and 1,804 women, of whom 4.8% had tuberculosis; the ratio of men and women was 2.5:1. In the literature it has been estimated that tuberculosis is from 5 to 10 times as frequent in diabetics as in the general population. The author found that in 1950 in West Berlin tuberculosis was four times more frequent in diabetic patients than in the general population. This patient material was unusual, since the incidence of tuberculosis had increased during World War II and the blockade in 1949. Following the lifting of the blockade in 1949 new cases and recurrences of diabetes increased considerably, particularly among women.

Ugeskrift for Laeger, Copenhagen

115:387-428 (March 12) 1953. **Partial Index**

Relation Between Number of Eosinophils in Blood and Bone Marrow Under Usual Conditions and Under Influence of ACTH. H. Uhrbrand. —p. 387.

*Effect of Mersalyl in Treatment of Pulmonary Stasis of Cardiac Origin Estimated by Determination of Vital Capacity. J. Marquardsen, J. P. Munck and F. Schulsinger.—p. 394.

Value of Cephalin Cholesterol Reaction as Liver Function Test. P. Grønback.—p. 399.

Effect of Diphenhydramine (Benadryl) Intravenously on Side-Effects in Intravenous Urography with Diodon. E. Gilg.—p. 404.

Penicillin Treatment of Erysipeloid. A. Ladehoff.—p. 409.

Hematuria After Cystoscopy with Rodalon Solution in Bladder. W. P. Sperling.—p. 412.

Effect of Mersalyl in Pulmonary Stasis of Cardiac Origin.—Marquardsen and his associates consider the administration of mersalyl a rational treatment in pulmonary stasis due to cardiac insufficiency. Of their 16 patients, 5 men and 11 women, aged from 48 to 79, 14 had myocardial degeneration on arteriosclerotic or hypertensive basis and two had mitral stenosis. In nine there was no peripheral edema, six had slight edema, and one patient had marked crural edema. From three to six injections of mersalyl or thiomerin were given, in the dosage of 2 ml. twice weekly. Treatment also included light rest in bed and restricted fluid and salt intake. In most of the cases there was loss of weight accompanied by increased vital capacity, usually with subjective improvement. The results seemed to be more certain in cases without peripheral edema. Measurements of the vital capacity were made by means of a pocket spirometer. The increase in vital capacity occurred within from five minutes to one hour after the injection.

115:439-478 (March 19) 1953. **Partial Index**

Symptomatology in Hypertrophy of Breast. J. Foged.—p. 439.

*Pulmonary Complications in Dysphagia. O. Jepsen.—p. 451.

Case of Acute Porphyria Treated with ACTH. C. Vogel. p. 455.

Varicella-Zoster. S. Dahl.—p. 459.

Training of Patients with Radial Paralysis. J. Thernøe.—p. 462.

Pulmonary Complications in Dysphagia.—Disorders localized in the throat may cause defective swallowing and overflow with aspiration of food and secretion from the esophagus to the air passages and lead to pulmonary symptoms, often with roentgenologic changes. Compression of the trachea due to goiter may cause tracheitis, from which a constant discharge gives rise to and maintains pulmonary symptoms. A further possibility for the origin of pulmonary complications in dysphagia is bronchial compression or involvement in esophageal dilatation or tumor. The pulmonary affection in dysphagia may be bronchitis, pneumonitis, fibrosis, inflammatory bronchostenosis, abscess, or empyema. Jepsen believes the syndrome to be considerably more frequent than the literature suggests. Eleven cases are reported, four of which are described in detail. The pulmonary affection usually appeared as a roentgenologically demonstrable infiltration, as a rule localized to the right lung. After treatment of the cause of the dysphagia, the pulmonary infiltrations sometimes receded. In most cases they failed to regress in spite of recovery from the primary disorder; in such cases fibrosis was believed to be present. By and large three groups are represented: (1) patients having pulmonary complications without manifest dysphagia, (2) patients having dysphagia without manifest pulmonary complications, and (3) patients with borderline cases. The first group is especially important, as acquaintance with the syndrome affords a possibility for earlier diagnosis and treatment of the primary disorder. The pulmonary symptoms connected with the dysphagia may at times be so marked that the dysphagia symptoms are forced into the background and are not mentioned by the patient except on close questioning.

Zeitschrift für Krebsforschung, Munich

59:1-166 (April 15) 1953. **Partial Index**

Relation of Hormones of Adrenal Cortex to Experimental Tumor Growth. R. Schober.—p. 28.

Atypical Mitoses in Walker Tumors and Their Cause. G. Bersch.—p. 44.

Behavior of Constituents of Tumor Cells in Transplantation: VI. Mitosis in Tumor Cells Following Injection of Cell Constituents of Same Type of Tumor. H. Lettré, F. K. Hemprich and B. Spirig.—p. 64.

Morphogenesis of Malignant Blastomas of the Lymphatic Apparatus Inclusive of Leukemia. S. Gräff.—p. 94.

Pathogenesis of Melanosarcoma and Problem of Malignant Degeneration on Basis of New Observations on 42 Tumors in Human Eyes. B. Davids. —p. 108.

*Dye-Stuffs Used in Coloring Foods: Question of Cancerogenesis. A. Wingler.—p. 134.

Cancerogenic Effect of Food Coloring.—Wingler points out that the increasing mechanization of food processing has led to the increasing use of coloring matter and other chemicals in foods. He discusses legal regulations existing in different countries with regard to the use of chemicals in foods, giving particular attention to the efforts made by German physicians to restrict and regulate the use of chemicals and coloring matter in foods. At the convention of German surgeons in 1949 a resolution was passed that basic food stuffs should not be colored, and in 1950 a committee was formed by the German research association to study the coloring of basic foods, in which coloring was not legally prohibited. The committee lists substances that thorough investigation has established as harmless, including among others certain "natural" coloring substances such as carotin, chlorophyll, and lactoflavin. The possible cancerogenic effect of substances used for the coloring of food stuffs has disturbed physicians ever since Japanese investigators in 1936 reported the development of tumors in rats that had been given dimethyl-amino-azobenzene, also known as butter-yellow (because of its use in the coloring of butter and fats). Procedures used in the testing of coloring substances that might prove cancerogenic are described and substances suspected of being cancerogenic are listed. In addition to prolonged feeding experiments on animals, the committee recommended studying coloring substances that are suspected of being cancerogenic with regard to the formation of Heinz bodies in the erythrocytes of cats. Dye-stuffs used in cosmetics and chemicals used in drinking water are likewise being investigated. The committee's chief object is to promote the collaboration between the industry that produces and uses the coloring substances, research bodies aiming to establish their harmlessness, and the legal authorities, so that the use of chemicals in foods will not be harmful to the consumer.

BOOK REVIEWS

J. Meller Ophthalmic Surgery: A Handbook of Surgical Operations on the Eyeball and Its Appendages. With supplement by K. Kofler. Translated and edited by Ray K. Daily, M.D., F.A.C.S., and Louis Daily, Jr., B.S., M.D., Ph.D. Sixth edition revised and enlarged by Professor Dr. J. Böck. Cloth. $12. Pp. 529, with 287 illustrations. Blakiston Company (division of Doubleday & Company, Inc.), 575 Madison Ave., New York 22, 1953.

The descriptions of various operative procedures are concisely and clearly written and are amply illustrated with drawings and photographs. With the gradual improvement in the technique of dacryocystorhinostomy, the indications for the classical Meller technique, however, are gradually becoming fewer. In the chapter on cataract surgery, the statement "Whoever has had experience of performing very many extracapsular extractions, with almost no complications, even in cases with quite immature cataracts, will naturally have but little inclination to change a reliable technique for a more daring procedure" gives the impression that the author prefers the extracapsular technique of cataract extraction. Like most European ophthalmic surgeons, he omits the retrobulbar injection and the generally accepted preplaced or postplaced corneoscleral sutures. The postoperative medication is brought up-to-date by the translators.

In view of the recent advances made with contact lenses and other optic aids, surgery of high myopia is no longer advisable because of its inherent risks and complications. Posterior sclerotomy preceding any definitive operation on an eye with a very high intraocular pressure is inadvisable, particularly since the use of hyaluronidase (in the procaine hydrochloride) in retrobulbar injection, produces practically the same result. In the chapter on corneal transplantation, the complications of slipping of the corneal disk and formation of anterior synechia are seldom encountered today. The more desirable method of edge-to-edge suturing of the graft to the recipient cornea permits early reformation of the anterior chamber.

This edition, like its predecessor, should be a preferred book on surgery of the eye, particularly with regard to operative procedures around the lids and for the classical Meller operation. The translators are to be congratulated on their magnificent piece of work and for the editorial notes that bring the text into more modern focus.

Handbook of Treatment of Acute Poisoning. By E. H. Bensley, M.B E., B.A., M.D., Director, Department of Metabolism and Toxicology, Montreal General Hospital, Montreal, and G. E. Joron, B.A., M.D., C.M., Junior Assistant, Department of Medicine and Department of Metabolism and Toxicology, Montreal General Hospital. Cloth. $2.50. Pp. 201. Renouf Publishing Company, Ltd., 2182 St. Catherine St. W., Montreal 25, Que., Canada, 1953.

This book was prepared as a guide to treatment of acute poisoning for physicians without special experience in toxicology and as a basis for instruction of students in the health professions and in first aid courses. It is divided into two sections, the first of which is devoted to basic principles, a general plan for treating acute poisoning, and discussions of individual methods of treatment. The second section describes common types of acute poisoning, with instructions for managing the patient before and after arrival of the physician. Brief notes on collection and preservation of samples for chemical analysis, a list of items for an emergency poison kit, and a brief list of recommended books on toxicology are presented in the appendix.

The authors state that, since the book is intended primarily as a guide to treatment of the acute poisoning emergency, certain aspects such as medicolegal problems, chronic intoxications, and the late consequences of acute intoxication are either avoided or mentioned incidental to the main discussion. No attempt is made to thoroughly cover agricultural, industrial, or household chemical products capable of causing injury, although a number of the commoner ones are indexed and grouped with related compounds with which the reader may be more familiar. Dosage recommendations are for adults, and the reader is advised to make appropriate modifications of doses when treating infants and children, with the warning that special care must be exercised in the use of morphine and picrotoxin for such patients. Small children, however, are the most frequent victims of accidental poisoning. Unfortunately, there is little reliable published information on dosages for children, and physicians must rely on experience or resort to empirical dosage rules based on age and weight. Since acute poisoning emergencies frequently call for special dosages, such information should be available in a treatment primer.

Renal Cortical Necrosis and the Kidney of Concealed Accidental Haemorrhage. By H. L. Sheehan, D.Sc., M.D., F.R.C.P., and H. C. Moore, M.D. Publication number 167, American Lecture Series, monograph in Bannerstone Division of American Lectures in Circulation. Edited by Irvine H. Page, M.D., and A. C. Corcoran, M.D. Cloth. $7.75. Pp. 186, with 64 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., [n.d.].

Renal cortical necrosis is a rare, though serious, condition seen frequently after an obstetric complication variously called premature separation of the placenta, abruptio placenta, or uteroplacental apoplexy. In all instances the fetus is killed by the hemorrhage within the uterus, and too frequently the mother dies of renal cortical necrosis from spasm of the renal vessels. In the past there have been several conjectures as to the cause of the condition; this led the authors to make a careful study of 67 autopsied cases.

The results of pathological examination of the kidneys and other organs in the 67 cases form the basis of the book. In many instances the autopsy was performed within two to five hours after death, and special precautions were taken to minimize the effects of pressure or distortion in removal of the organs. There are a number of excellent photomicrographs of kidney sections showing all stages of change, from cloudy swelling to spasm, to thrombosis and later healing. Correlative clinical and histological analysis made it possible for the authors to postulate with considerable certainty the sequence of events in renal cortical necrosis. Damage to the kidney takes place very quickly after the onset of the uterine hemorrhage. Initially, there is spasm of the malpighian glomerulus, which is followed after a few minutes to five or more hours by complete cessation of blood flow to the glomerulus. After this period, a relaxation of spasm takes place, and blood recirculates. When there is a short period of spasm, minor changes are seen in the tubules and other portions of the kidney. Cases of this type are mild, showing proteinuria and casts, and the kidney soon returns to normal function. Severer cases have a secondary spasm of a part of the intralobular artery and progress to renal cortical necrosis. Between these extremes there are many clinical and pathological types. When the spasm relaxes, blood flows to the parts and is promptly thrombosed, thus arresting all further circulation to the part. Release of the spasm within the first two or three hours after the original stoppage of blood flow will prevent gross renal lesions from developing. The authors give no hint as to the probable cause of the original spasm.

The book is well written and readable. The 14 chapters cover the important phases of the condition and, to an adequate extent, related conditions. A full bibliography and an excellent index make it possible to find references in both the literature and the book. It is written primarily for specialists in obstetrics and pathology, and it should be favorably received as a much-needed work in a previously obscure area of information.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Morris' Human Anatomy: A Complete Systematic Treatise. Edited by J. Parsons Schaeffer, A.M., M.D., Ph.D. Contributors: Leslie B. Arey, et al. Eleventh edition. Cloth. $16. Pp. 1718, with 1220 illustrations. Blakiston Company, 575 Madison Ave., New York 22, 1953.

This well-known textbook of anatomy continues to bear the name of its originator, Sir Henry Morris, a distinguished surgeon and teacher, born and educated in England, a president of the Royal College of Surgeons, a member of the General Medical Council, one of the founders of the Imperial Cancer Research Fund, a president of the Section on Anatomy and Histology of the British Medical Association, and an honorary member of the Medical Society of the State of New York. Sir Henry was editor of the first, second, and third editions and coeditor of the fourth edition with J. P. McMurrich of the University of Michigan. From the 5th edition through the 9th, the editor was C. M. Jackson of the University of Michigan, who was followed by J. P. Schaeffer of Jefferson Medical College for the 10th edition and the present edition. Many other authorities, both British and American, have contributed sections to the various editions. New contributors are Ernest Lachman, who collaborated with Raymond F. Blount in preparation of the section on the digestive system; J. E. Markee, author of the section on the urogenital system; C. G. Smith, who collaborated with J. C. B. Grant in revising the section on the musculature; and Mildred Trotter, who with Robert J. Terry rewrote and revised the sections on osteology and the articulations. The other contributors to this edition are the same as in the preceding edition.

Many illustrations have been replaced with new ones, and illustrations have been added, including a number of roentgenograms. To keep the text within a single volume, some items have been set in smaller type and made up in double columns for easier reading. Much investigation remains to be done in anatomy. Recent studies in this field have made certain previous descriptions untenable, and it becomes necessary from time to time to rewrite and revise. That has been well done in this volume. A better grade of paper and less of the smaller type would have contributed to ease of reading.

Die Lungenresektionen. Von Prof. Dr. A. Lezius, o.ö. Professor der Chirurgie an der Universität Hamburg, Hamburg. Mit einem Geleitwort von Prof. Dr. R. Nissen, Director der chirurgischen Universitätsklinik Basel. Cloth. 49.80 marks. Pp. 143, with 149 illustrations. Georg Thieme Verlag, Diemershaldenstrasse 47, (14a) Stuttgart-O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., N. Y. 16, 1953.

This is the first of a series of monographs dealing with thoracic surgical problems. Radical surgical extirpation is stressed as the treatment of choice in neoplasms of the lung; however, no such specific therapy can be recommended regarding inflammatory lesions of the lung. Specific indications for removal of a lung, lobe, or segment still differ. It is important, nevertheless, to standardize techniques for such procedures before results can be properly evaluated according to the test of time. The author has also included short, terse sections on diagnosis, indications, and preoperative and postoperative care; these factors cannot be thoroughly separated from operative technique.

Only one of such great experience and unusual technical skill could state that a standardized technique of pulmonary resection does not exist. Techniques are altered by the temperament and dexterity of the surgeon as well as by the numerous physiological anomalies that continually plague, yet stimulate, him. The techniques described are based on the author's experience with 1,000 cases. It is refreshing to note that, in this day of many gadgets, he uses no special armamentarium, since he believes that success of the operative procedure depends on the head and hands of the surgeon rather than on instruments.

The art work by Ingrid Schaumburg is outstanding. These beautiful illustrations reveal the close collaboration that must exist between author and artist if the "feel" of the operating room is to be truly depicted. This book is an outstanding example of authoritative teaching and brillant presentation. It is recommended to anyone interested in lung resections.

The Epidemiology of Health. Iago Galdston, M.D., editor. New York Academy of Medicine Book. Cloth. $4. Pp. 197. Health Education Council, No. 10 Downing St., New York 14, 1953.

Epidemiology is an old discipline that has been associated, in the minds of physicians, with disease and its control. Epidemiology of health is a startling term to the casual reader, but the members of this symposium, referring to history, have shown that for centuries there has been an epidemiology of health as well as an epidemiology of disease. This positive concept expressed in the phrase "a healthy mind in a healthy body" and in the concept of health "as physical, emotional and spiritual well-being rather than mere absence of disease" has been a long-sought goal.

This volume records 15 papers that were the subject matter of the Eleventh Annual Eastern States Health Education Conference. The concept of a positive epidemiology of health is discussed by well-informed physicians in terms of its history and evolution and the way it is currently applied to health practice in the Army, in industry, in tuberculosis, in mental hygiene, in nutrition, and in some of the newer concepts such as geriatrics, preventive medicine in private practice, and public health and health education.

This stimulating book should be read by physicians who are concerned with the attitudes that are developing toward disease and the relation that medical practice has to such special fields as preventive medicine, public health, and the care of the healthy. The foreword is by Howard R. Craig, director of the New York Academy of Medicine, and the first chapter is by Iago Galdston of the New York Academy of Medicine, who also served as editor for the symposium.

Archiv und Atlas der normalen und pathologischen Anatomie in typischen Röntgenbildern: Einführung in die Enzephalographie (Pneumenzephalographie). Von Dr. med. habil. Otto Schiersmann, Dozent für Neurologie und Psychiatrie, Chefarzt des Krankenhauses Bethesda, Wuppertal-Elberfeld. Ergänzungsband 64, Fortschritte auf dem Gebiete der Röntgenstrahlen vereinigt mit Röntgenpraxis, herausgegeben von R. Grashey, et al. Second edition. Cloth. 36 marks. Pp. 135, with 192 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

This is the second and enlarged edition of an introductory monograph on pneumoencephalography that first appeared in 1942. The book deals first, briefly, with the anatomy of the ventricular system and the intracranial subarachnoid spaces and the physiology of the cerebrospinal fluid. Various means of filling the ventricular system (ventricular, suboccipital, and lumbar puncture) and the different contrast media employed in visualizing the ventricular system are discussed. The author prefers the injection of air by the lumbar route, although he has used the suboccipital route extensively. The technique of obtaining satisfactory films and their interpretation occupy the remainder of the text. The illustrations are satisfactory.

This little monograph is truly introductory and cannot be compared to the much more thorough presentations of the subject. There is an index and an extensive bibliography. The latter would be far more useful, however, if the German practice of presenting the references one immediately after the other were abandoned for the arrangement of the authors' names in a column.

Lust-Pfaundler-Husler Krankheiten des Kindesalters: Ihre Erkennung und Behandlung in der Praxis. Von Prof. Dr. Josef Husler, Chefarzt des Kinderkrankenhauses München-Schwabing. Nineteenth edition. Cloth. 29.80 marks. Pp. 700. Urban & Schwarzenberg, Thierschstrasse 11, München 26; Meinekestr. 13, Berlin W. 15, 1953.

Professor Husler has revised and edited this edition somewhat after the plan followed by the editors of Osler's "Practice of Medicine." The volume is in three parts. The first is a survey of the entire field of pediatrics, including diseases of the newborn and infections in the growing child. The second part deals with diagnosis and treatment from the technical viewpoint. Part 3 concerns methods of feeding, including diets auxiliary to milk. There are 155 pages devoted to alphabetic listing of drugs and discussions of poisoning. Special attention is given to congenital defects in the heart and circulatory system, to virus pneumonias, and to the use of antibiotics, including contraindications. This comprehensive book will be useful to general practitioners who read German.

Office Orthopedics. By Lewis Cozen, M.D., F.A.C.S., Assistant Professor of Orthopedic Surgery, College of Medical Evangelists, Los Angeles. Second edition. Cloth. $5.50. Pp. 304, with 191 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1953.

This book actually covers the whole field of orthopedics, at lease with reference to diagnosis. Cases that would be treated in the office have a much more extensive diagnosis and differential diagnosis, while those that would of necessity be hospital cases are mentioned briefly, since these should not be considered a part of office practice of orthopedics. Many of the procedures mentioned can be done in the office if the necessary equipment is at hand; however, a considerable amount of such work is usually done at the hospital.

This edition is up-to-date with regard to treatment and refers to many new methods or new drugs that have been announced within the last six months. While most of the outlined treatment is generally accepted, all of the suggested methods of treatment are not universally accepted, and several are definitely controversial. Many of the drawings and illustrations are borrowed from other books or texts, so that there is a great deal of review rather than original work. This book is chiefly for physicians doing general surgery or in general practice who need a ready reference to office orthopedics; however, the descriptions in the book are inadequate for its use as a textbook of orthopedic surgery.

Gout and Gouty Arthritis. By John H. Talbott, M.D., Professor of Medicine, The University of Buffalo School of Medicine, Buffalo, New York. Modern medical monographs, 7. Cloth. $4. Pp. 92, with 32 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1953.

This monograph is the result of 20 years of laboratory investigation on uric acid metabolism and clinical study of gout. The more recent biochemical advances in this field are recorded, with emphasis on clinical aspects.

Most of the phases of gout are covered briefly. Of particular interest is the discussion of intermediary metabolism of uric acid, which includes a review of the precursors of uric acid, the miscible pool, and turnover rate of labeled uric acid. Of equal interest is the section on concentration of urates in serum and renal exchange of urates. A discussion of probenecid (Benemid), a uricosuric agent, is well presented. The remainder of the material covers symptoms, diagnosis, and treatment of gout.

While the roentgenograms are good, their value would have been enhanced if photographs had been included to coincide with the various roentgenologic phases. The bibliography is fairly comprehensive. The material is accurately presented, although the theory that a liberal intake of protein has no effect on the course of this disease is not entirely acceptable. The book is well written, easy to read, and is highly recommended to those interested in gout and gouty arthritis.

Lind's Treatise on Scurvy: A Bicentenary Volume Containing a Reprint of the First Edition of a Treatise of the Scurvy by James Lind, M.D., with Additional Notes. Edited by C. P. Stewart, Ph.D., D.Sc., and Douglas Guthrie, M.D., F.R.C.S.E. [Originally printed by Sands, Murray, and Cochran, Edinburgh, for A. Millar, in the Strand, London, 1753.] Cloth. 45s. Pp. 440, with 4 illustrations, Edinburgh University Press, Old College, South Bridge, Edinburgh 8 [sole agent: Oliver & Boyd, Ltd., Tweeddale Court, 14 High St., Edinburgh 1], 1953.

Although this book was published 200 years ago to demonstrate that scurvy could be prevented and cured, it is still surprisingly modern in outlook and in literary style. Lind's treatise on scurvy not only led to the virtual disappearance of the disease in civilized communities, but through its presentation of the subject, with censure of muddled thinking and superstition, emphasis on careful observation and controlled experiment, and reliance on facts and rational interpretation of them, it has attained recognition as one of the great medical classics of all time. The reprinting of this book, together with additional notes giving a short biography of Lind and a summary of the present status of vitamin C, pays tribute to a man who received little attention during his life. This is an eminently readable book and deserves careful study.

Patients Are People: A Medical-Social Approach to Prolonged Illness. By Minna Field. Cloth. $3.75. Pp. 244. Columbia University Press, 2960 Broadway, New York 27; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, 1953.

Many years experience as a social service worker in a large chronic disease hospital (Montefiore Hospital, New York) form the background of this author. She has found that the problems of chronic illness are complex from all points of view, medically, socially, and psychologically. Montefiore Hospital for many years has acted as a sort of a laboratory in trying out new methods of caring for the patient with a long illness. For instance, the home care now carried on in many cities was initiated at Montefiore Hospital in 1947. How to handle the rapidly increasing number of chronically ill and aging patients as a family or community problem still defies adequate solution; therefore, many methods must be tried out on a pilot scale for the next several years. It would be a mistake, as the author points out, to set up a rigid over-all scheme on a national level at this time. The many facets of this gigantic medicosocial problem are competently and dispassionately discussed. This book should be read by all who are interested in human aspects of chronic illness.

Die geburtshilflichen Operationen: Ihre Ausführung und Anwendung, ein Lehrbuch für Studenten und Gebrauchsbuch für Ärzte. Von Prof. Dr. Med. Heinrich Martius, Direktor der Universitäts-Frauenklink Göttingen. Seventh edition. Cloth. 34 marks. Pp. 290, with 268 illustrations. Georg Thieme Verlag, Diemershaldenstrasse 47, (14a) Stuttgart-O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., N. Y. 16, 1953.

In spite of the fact that successive editions of books on operative procedures become larger and contain more illustrations, this one is not larger than the last and contains 13 less illustrations. This is because modern operative obstetrics has become simplified, and several surgical procedures have become obsolete. The changes in this edition are not many, presumably because operations in obstetrics have not changed much, nor have there been any significant surgical advances in obstetrics. This small book is full of excellent advice concerning the indications for, and the technique of, practically all obstetric operations. The vast experience of the author as a practicing obstetrician and as a teacher is evident throughout the book. The illustrations are clear, instructive, and numerous. For anyone who can read German, this book is highly recommended.

Food for Your Heart: A Manual for Patient and Physician. By Department of Nutrition, Harvard School of Public Health, Harvard University, Boston. This manual has been reviewed and endorsed by Council on Foods and Nutrition, American Medical Association. Paper. 25 cents. Pp. 48. American Heart Association, Inc., 44 E. 23rd St., New York 10, 1952.

The busy physician pressed for time to explain the "whys" and "wherefores' of necessary diet restrictions to his patients with cardiac conditions will welcome this booklet of the American Heart Association. Useful facts and practical directions are presented in simple, nontechnical language easily understood by the average patient. Tables of the sodium content of foods and water supplies are included in the appendix. This manual, prepared by the Department of Nutrition at Harvard University, has been reviewed and accepted by the Council on Foods and Nutrition of the American Medical Association.

Einführung in die pathologische Physiologie. Von Professor Dr. Max Bürger, Direktor der medizinischen Universitätsklinik Leipzig, Fourth edition. Cloth. 42 marks. Pp. 561, with 193 illustrations. Georg Thieme, Thomaskirchhof 21, (10b) Leipzig, C. 1, 1953.

Impressive both in appearance and in content, this book covers thoroughly the field of functional disturbances of the various systems of the body. The author assumes that his readers are solidly grounded in anatomy, physiology, and biochemistry, but he provides a wealth of illustrations, tabular data, and chemical information for the benefit of those whose command of these subjects is weak or not up-to-date. The broad pages are not easy to read; a two column page would be preferable. There is a good index. The book can be recommended as comprehensive, scholarly, and modern.

QUERIES AND MINOR NOTES

TREATMENT OF HYDROFLUORIC ACID BURNS

TO THE EDITOR:—*Please give an opinion on the use of "triple dyes" and calcium gluconate locally for the treatment of hydrofluoric acid burns. I have had misgivings about the routine use of calcium gluconate in such places as the finger tips, especially when the burns are believed to be mild.*

John E. Maley, M.D., Ann Arbor, Mich.

ANSWER.—The following treatment is based on the experience of a consultant who, over a four year period, observed from 10 to 20 burns a week of varying degrees caused by hydrofluoric acid of varying strengths. The treatment as finally elaborated produced no deformities, disabilities, or compensation losses over more than two years. Such a program involves prompt treatment with water at the place where the accident occurred and removal of the patient to the medical department, where judgment is made as to the extent of further treatment necessary. The success of this treatment lies in the emphasis on meticulous care during the initial stages. This experience has resulted in a refusal to make a judgment as to definitive treatment until at least 24 hours have elapsed. In essence, the treatment consists of immersion in water (never a neutralizer) for not less than 30 minutes and up to four hours. This is followed by application of packs saturated with glycerin, which are changed every four hours. On the second day, the burns can be classified as to whether further damage will occur or only dressing changes will be needed for a day or two. Because hydrofluoric acid has a tendency to prolong its action on the tissues for four or five days, in contrast to other acids, this decision on the second day is extremely important. The patient is always given the benefit of any doubt about whether the burn is progressive. If the decision is made that the injury could result in a second or third degree burn, further treatment consists of meticulous cleansing of the areas involved according to surgical standards and use of the compression techniques described by Blair, Koch, and Mason. Ample quantities of finely powdered tantalum oxide is blown on the area with special apparatus. The tantalum oxide powder has no bacteriostatic or bactericidal properties, but, on the other hand, it cannot possibly enter into a chemical reaction with any of the body tissues or fluids. It is, therefore, as nonirritating a dressing as could be used. In addition, a physical factor is involved in its use in that this powder, which has been passed through a 400 mesh screen, has enormous surface area and creates tremendous capillary attraction when applied to oozing wounds. Any such oozing creates a tough, nonirritating cover when tantalum oxide is used. The dressing applied on the 2nd day by the compression technique is not removed until the 9th or 10th day.

This consultant stopped using calcium gluconate injections locally, because, in the majority of his cases, such injections contributed to sloughing, which resulted in the need for plastic surgery in many cases. Burns underneath the finger nails present a distressing problem because of the physician's tendency to delay treatment in the hope for spontaneous improvement. It is far better to do a fairly radical removal of the distal third of the nail whenever a patient complains of pain in that region than to procrastinate in the hope that the pain will go away. Such surgical removal of the nail gives immediate relief. In eye burns, initial treatment with water for not less than four hours will prevent injury if such treatment can be started within 15 to 30 minutes after the acid has entered the eye. Under no circumstances is the use of any neutralizing solution advocated. The use of triple dyes was discarded by this consultant more than 20 years ago. There are much better ways to promote wound healing than by the use of antiseptics of that nature.

CORTISONE OR CORTICOTROPIN IN RHEUMATIC FEVER

TO THE EDITOR:—*Is it wise to give cortisone or corticotropin (ACTH) to all patients with acute rheumatic fever?*

M.D., Utah.

ANSWER.—Determination of the exact phase of rheumatic fever during which administration of cortisone or corticotropin can be expected to produce best results has not been achieved. Effects observed from use of these hormones in rheumatic fever are as follows: suppression of fever, amelioration of polyarthritis, slowing of tachycardia, improvement of the "toxemia," improvement of appetite, lowering of the erythrocyte sedimentation rate, improvement of atrioventricular conduction, improvement of anemia, and restitution to normal of abnormal levels of blood proteins. Much time will be required before a determination can be made of the effects induced by these hormones on eventual cardiac lesions. Important observations reported since announcement of the original discovery include the following ones: properly administered, these hormones may cause reduction in the size of the heart; if withdrawn prematurely, reactivation of the rheumatic process may occur; recurrences are not prevented; preexisting organic murmurs are not abolished; signs of pericarditis, with or without effusions, may disappear rapidly; chorea, when present, has been observed to disappear promptly; subcutaneous nodules may soften, diminish in size, or disappear during periods of administration of these compounds; congestive heart failure accompanying acute rheumatic fever may improve; and in some instances, cardiac murmurs associated with dilation of the heart disappear rapidly. The latter effects may result from the anti-inflammatory effect of cortisone or corticotropin on the myocardium, and thus, congestive heart failure is not a contraindication to the use of these hormones.

With these principles in mind, general rules may be suggested on which to make decisions about use of cortisone or corticotropin in treatment of rheumatic fever. It seems reasonable that these hormones be used in instances in which attacks are severe, that is, when fever is notable, when joints are considerably swollen and painful, when tachycardia is present, the leukocyte count is elevated, and electrocardiograms disclose disturbances of conduction. Either cortisone or corticotropin should be administered in acute rheumatic fever in adequate doses and should be given for at least four to six weeks, if possible. Consideration should be given to the metabolic disturbances these hormones induce. Salt intake should be limited, adequate amounts of proteins should be made available, and precautions should be taken to prevent excessive gain in weight due to a large intake of calories. When the time arrives for withdrawal of cortisone or corticotropin, this should be undertaken slowly rather than abruptly. The dose should be lowered by decrements of 12.5 to 25 mg. of cortisone or 15 to 10 units of corticotropin. If signs appear suggesting that the disease is becoming reactivated, the dose should again be increased for periods of several days to several weeks. Subsequently, the amount administered should again be gradually reduced. In general, before administering cortisone or corticotropin to a patient with acute rheumatic fever, the physician should observe the patient for a few days. The attack may clear spontaneously, that is, febrile temperatures may return to normal, rapid pulse rates may become slow, elevated leukocyte counts and sedimentation rates may return to normal, and toxicity and arthralgias may disappear with little treatment other than bed rest.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ABORTIONS AND EXPOSURE TO LEAD

To the Editor:—*A patient has just had her second spontaneous abortion, both at three and one-half months gestation; the first occurred in June, 1952, the second in March, 1953. During her second pregnancy, she was taking prophylactic Proloid (a thyroid preparation) and diethylstilbestrol. Her last menstrual period occurred Nov. 4, 1952. She had no symptoms of abortion until the event took place with typical bleeding and cramps. She has been working with lead styphnate and butyl acetate since November, 1950. Could there be any connection between the abortions and the patient's exposure to these chemicals?*

M.D., New York.

Answer.—Lead could have induced the abortions, provided sufficient exposure occurred, but it is recognized that other causes could have operated in bringing them about. If this patient has resumed work, it may prove possible to appraise the extent of exposure. Since lead styphnate commonly is handled in small quantities and sometimes wet, determination of lead in the general workroom atmosphere may be without value. The exposure, if any, is likely to be sharply local and may represent "hand-to-mouth" transfer, even though gloves may have been worn. Particularly if this patient has resumed work, but even if she has not, the urinary level of lead should be determined. In addition, although it is not a conclusive test, examination for cellular stippling on a quantitive basis should be done, and the basophilic aggregation test should be conducted. If other persons are engaged in identical work, some or all should be tested for lead in the urine and blood; however, negative results in other employees may not be significant, since exposure may have been strictly individual. Exposure to lead on the part of the husband would be significant and should be determined.

EXTRASYSTOLES

To the Editor:—*A 40-year-old physician has had ventricular extrasystoles for five years. Complete examination has not revealed any pathological condition. Electrocardiograms made by different cardiologists show the extrasystoles to be irregular in frequency (every 4, 6, or 12 beats) and especially strong in the supine position. There have never been signs of myocardial damage. The gastrointestinal tract was examined roentgenographically, with no abnormal findings. The patient's activities are undisturbed; however, these premature beats have become annoying, and the patient has to take 3 grains (0.19 gm.) of quinidine three or four times a day to eliminate them. As soon as he stops treatment, they return. 1. Can quinidine in this amount be taken without harm over a long period? 2. If the heart becomes refractory to quinidine, what other drug can be used? 3. Will this condition cause, in the long run, any other cardiac disturbance? 4. What else besides quinidine and psychotherapy might be of benefit to him?* *M.D., New York.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—1. Quinidine can be taken over an indefinite period without cumulative toxic effects, other than the acute effects that can result from overdosage. 2. The use of quinidine is not characterized by the development of refractory states. It is unlikely that the patient's heart will become refractory to it. 3. There is no definite evidence that extrasystoles of the type described cause myocardial damage or any other cardiac disturbance leading to shortening of life expectancy. 4. Other suggestions, in addition to use of quinidine and psychotherapy, that might be helpful include (*a*) the use of a mild sedative, such as barbiturates and bromides; (*b*) abstinence from use of coffee, strong tea, cola drinks, and tobacco, any one of which may aggravate extrasystoles; in addition, extrasystoles may be aggravated in some patients by various forms of alcoholic beverages, whereas in other patients these factors seem unimportant; (*c*) it is suggested that these patients make a point of getting at least eight hours sleep at night so that they are not unduly nervous from chronic fatigue.

Answer.—The problem of ventricular extrasystoles is frequently encountered. 1. Quinidine taken in amounts of 3 grains three or four times daily can be taken without harm over such a long time, especially since this patient seems to have experienced none of the usual disagreeable sensations following its prolonged use, such as tinnitus, vertigo, and nausea. Commonly, 1 grain (0.06 gm.) taken three to five times daily will be found as effective as the larger doses mentioned. 2. There is a possibility that after prolonged use quinidine will lose its effectiveness; however, discontinuing use of the drug for one month usually restores its effectiveness. 3. In this consultant's experience, premature ventricular contractions on a nonorganic basis have not resulted in myocardial damage. Such an arrhythmia, however, if projected over a long period, frequently becomes progressively aggravated and more refractory to management. 4. Most premature ventricular contractions (extrasystoles) have an activating, exciting, or instigating factor. In this case, the gastrointestinal tract was found normal on several roentgenographic examinations; however, other sources of infection must be ruled out, notably the gallbladder, nose, throat, mouth, and teeth. More important is a careful study of the patient's habits. Tobacco is a frequent cause of ventricular extrasystoles. Alcohol, strong coffee, and tea are frequently responsible. Pent-up emotions, worry, and fear are common causes, in which case the proper management is psychiatric plus the use of mild sedation in conjunction with quinidine.

EMERGENCY TREATMENT OF ADRENOCORTICAL INSUFFICIENCY

To the Editor:—*In Queries and Minor Notes in* The Journal *March 7, 1953, is a discussion on cortisone administration, in which it is stated that when certain conditions of stress ensue in the wake of previous cortisone therapy the drug be readministered to counter effects of suppressed adrenocortical function. Severe intercurrent infection is mentioned as such a stress situation. I have gained the impression from published reports of animal experiments that minor infections may become overwhelming in the presence of cortisone. If this is the case, it occurs to me that in the presence of infection another form of substitution therapy might be more beneficial. Can you clarify this for me?*

Roger D. McKenna, M.D., Madison, Wis.

Answer.—In the event of increased stress, such as might be caused by severe infection, burn, a surgical procedure, traumatic injury, hemorrhage, or other form of shock, the patient who also has adrenocortical insufficiency must be supplied exogenously with an adequate quantity of adrenocortical hormones. This applies whether the adrenocortical insufficiency is temporary, as in the case of rheumatoid patients who have been receiving cortisone, or permanent, as in Addison's disease. At present, the most expeditious way to supply such patients with adrenocortical hormone usually is to administer cortisone; extra salt and desoxycorticosterone also are necessary in some cases of sodium and chloride depletion not adequately managed by the administration of cortisone alone. If the patient has been receiving corticotropin the dose may be increased during the period of stress, if the adrenal cortexes are capable of responding; however, administration of corticotropin alone does not constitute adequate emergency treatment of adrenocortical insufficiency when the adrenal cortexes are temporarily atrophic, since several days of stimulation by corticotropin may be required to achieve adequate production of adrenocortical hormones. The dosage of cortisone is of greatest importance in this problem. Grossly excessive doses, such as were used in the animal experiments probably referred to in the query mentioned, do interfere with the normal reaction of tissues to infection; however, doses in the range of the body's requirement for the particular stress do not impair but rather strengthen the body's defenses. Unfortunately, the exact requirement of adrenocortical hormones at any one time cannot be precisely determined in advance; doses must be adjusted to fit the varying circumstances in the case. In general, doses of cortisone between 100 and 200 mg. per day have been found

effective in preventing adrenocortical insufficiency in the event of most stresses and have been employed during the relatively brief course of severe acute infections without apparent aggravation of the infections. Even larger doses may be used for short periods, if needed to prevent adrenocortical insufficiency. Appropriate specific treatment for the infection, such as antibiotic therapy, chemotherapy, or surgical drainage, should be instituted. As these measures bring the infection under control, the dose of cortisone should be reduced gradually. Current information does not suggest that any presently available adequate substitute for cortisone, for example, hydrocortisone or large doses of adrenocortical extract, would be appreciably superior to cortisone in the management of problems of this sort.

RHEUMATOID SPONDYLITIS

To the Editor:—*A patient with spondylitis anklopoietica (Marie-Strümpell disease) also has sinusitis, and hemolytic streptococci and staphylococci have been cultured from the sinus lesions. Would a trial of autogenous vaccine be in order? Please discuss the etiology of this disease.*

M.D., Florida.

Answer.—No unanimity of opinion prevails about the use of vaccines in the treatment of articular diseases. Most rheumatologists no longer use either autogenous or stock vaccines, because the results have not been encouraging on critical evaluation; however, some physicians do still use vaccine therapy, and a trial of either an autogenous or stock vaccine would not be contraindicated in the case described. Before treatment with a vaccine is considered, specific treatment of the infection of the sinuses, including use of appropriate antibiotics and establishment of adequate drainage from the sinuses, is indicated.

Rheumatoid spondylitis (a term proposed by the American Rheumatism Association in preference to "Marie-Strümpell's arthritis") is an inflammatory, probably nonspecific disease affecting principally the sacroiliac joints and diarthrodial joints ("facets") of the spinal column. As in other rheumatoid diseases, the inflammatory process also may affect the periarticular, fibrous, and other mesenchymal tissues of the body. The etiology of rheumatoid spondylitis remains unknown. Comprehensive studies have indicated that many of the previously suggested concepts of its cause are not tenable at present. An ill-considered notion that rheumatoid spondylitis is due to hyperparathyroidism was apparently based on the prominence of calcification of vertebral ligaments with an associated osteoporosis of the vertebral bodies. This theory was at its zenith about 20 years ago but is now discarded. Another idea, also discarded, was that rheumatoid spondylitis is due to gonorrheal infection. This was probably proposed because of the tendency for both diseases to occur in young adult males. It also has been thought that rheumatoid spondylitis might be the result of focal infection, tuberculosis, or other infection of the sacroiliac joints or congenital anomalies of the lumbosacral segments of the spinal column, but these remain unproved and unlikely explanations.

Although injuries of varying extent to the back are apparently a common experience of both men and women, trauma cannot usually be related to the onset of rheumatoid spondylitis. Studies by Shands and Oates at Duke University and by Golding in England as well as by others interested in rheumatoid spondylitis have supported this observation. The onset of rheumatoid spondylitis could be related to trauma in only 7% of more than 1,000 cases studied at the Mayo Clinic by Polley. Most European rheumatologists are of the opinion that rheumatoid spondylitis is unrelated to rheumatoid arthritis of peripheral joints, but the consensus among most American rheumatologists is that these diseases are closely related to each other. Twenty-five to 50% of patients with rheumatoid spondylitis have associated arthritis of peripheral joints that is indistinguishable both clinically and pathologically from rheumatoid arthritis of peripheral joints seen in patients without rheumatoid spondylitis. Although the cause of rheumatoid arthritis also remains to be established, the prevalent opinion about the cause of rheumatoid spondylitis is summarized in the statement that "presumably, but not certainly, the cause of rheumatoid spondylitis is the same as that of peripheral rheumatoid arthritis" (Hench, P. S.; Slocumb, C. H., and Polley, H. F.: *M. Clin. North America* **31**:879, 1947).

COMPETITIVE ATHLETICS FOR HIGH SCHOOL STUDENTS

To the Editor:—*Do you have information regarding the danger of the occurrence of cardiac hypertrophy, with permanent heart damage, owing to the strenuous physical exertion of competitive swimming at junior high school and high school levels?* *Stephen S. Ellis, M.D., Coffeyville, Kan.*

Answer.—Few controlled studies are available on the effect of strenuous physical exertion on the heart of normal youths of junior high school and high school ages. There is even less dependable information on the effects of swimming. No report of death from competitive swimming was found in a review of the literature from 1945 to the present. Best and Taylor (The Physiological Basis of Medical Practice, ed. 4, Baltimore, Williams & Wilkins Company, 1945) state, "It is now agreed that cardiac enlargements are the result of pre-existing disease and the normal heart cannot be dilated beyond its physiological limit, nor will a bout of strenuous exercise 'strain' the healthy heart muscle or cause it to fail. . . ." In a 1945 report of the Committee on the Cardiovascular Study of Athletes, Wolffe and Mueller state, "Unquestionably it is injudicious to allow on a school team students with a limited cardiac reserve shown, for instance, by a history of rheumatic fever and evidence of damage to some important part of the heart. . . ." (The Heart of the Athlete, Report of the Committee on the Cardiovascular Study of Athletes, Philadelphia, 1945). Smith (*Proc. Staff Meet., Mayo Clin.* **10**:122, 1935) states, "The point I want to emphasize is that strenuous physical exercise and hard manual labor do not cause, or predispose to, heart disease; that such activities do not cause abnormal cardiac hypertrophy and that the athletes do not develop early disability and die because of exercise they indulged in while in school." Johnson, Brouha, and Darling stated in *Revue canadienne de biologie*, June, 1942, "We have had many years' experience in working normal healthy young men to exhaustion on the treadmill, rowing machine or bicycle-ergometer and have never observed any undesirable sequelae." In the Report of the Joint Committee on Athletic Competition for Children of Elementary and Junior High School Age, published by the American Association for Health, Physical Education and Recreation, in 1952 (Washington, D. C.), a questionnaire study of physicians' reactions to athletics for children is tabulated in terms of a number of health factors. Of the 220 physicians expressing an opinion, only two (0.9%) considered competitive swimming not advisable for children 12 to 15 years of age. This suggests that swimming is not considered a hazardous competitive sport by the physicians queried. It would appear from the evidence available that normal children in the 7th to 12th grades can safely compete in swimming, provided they are safeguarded by medical examinations that give reasonable assurance of no abnormal heart condition and they are supervised by a competent coaching staff.

HOT FLASHES LONG AFTER THE MENOPAUSE

To the Editor:—*Hot flashes sometimes are complained of 5, 10, or even 15 years after the cessation of menstruation. What is the explanation, and is there any special treatment beyond the sparing use of estrogens?*

D. A. MacGregor, M.D., Wheeling, W. Va.

Answer.—The vasomotor symptoms of the menopause are due to the inevitable endocrine readjustment following the cessation of ovarian function. The query does not state whether this patient has been given estrogens, but there is no doubt that too persistent therapy of this sort, putting into the woman's circulation what nature is trying to get rid of, defers the inevitable readjustment. Estrogen therapy, if it has been used, should be discontinued, and the chief reliance should be on psychotherapy and simple sedatives.

PRIMARY TUBERCULOSIS

To the Editor:—*1. Is primary hilar tuberculosis considered infectious? Should a child with primary tuberculosis be admitted to a general pediatric ward? 2. What is the point in examining gastric juice in primary tuberculosis? If an acid-fast bacillus is found or if the injected guinea pig dies of tuberculosis, is this proof that the patient is infectious to others? 3. Two asymptomatic children are Mantoux positive. One shows no roentgenographic changes and the other a large mass of hilar nodes. Is there any difference in their infectivity to others? Is there any difference in their prognosis? 4. A child, aged 2 years, lives in an orphanage. His father has open tuberculosis. The child is symptomless and has no roentgenographic changes but had a Mantoux conversion three months ago. Should he stay at the orphanage or be admitted to a hospital? Another child, aged 6 years, had a Mantoux conversion nine months ago and has a large hilar flare without symptoms. Should he stay at the orphanage? 5. Is there good evidence that rest is beneficial in the treatment of primary tuberculosis, even if large hilar nodes are present? Provided children are not fatigued, is it not better to treat them as outpatients rather than admit them to a hospital, especially since they get no specific chemotherapy? 6. Frequently one hears that children with primary tuberculosis should have routine lumbar punctures to detect cases of meningitis early. May not this procedure cause meningitis by releasing the pressure on a tiny unsuspected subcortical tubercle so that the tension inside it causes it to rupture into the cerebrospinal fluid?*

S. Levin, M.D., Boston.

Answer.—As far as possible, the answers will be given categorically as the questions have been asked: 1. Primary hilar tuberculosis is not necessarily considered infectious. Open pulmonary lesions must also be present before bacilli can escape into the bronchial secretions. It is true that Ranke claimed that lymph nodes along the main bronchi may discharge bacilli into the bronchi by a "leakage" process, which he called "hilus catarrh." Leakage from the large nodes at the hilum would, however, be rare, and any such "leakage" would contain so few bacilli that they would probably never get past the lips to infect others, although they may be found in the gastric washings. Children with primary tuberculosis may be admitted to pediatric wards, but quarantine techniques should be carried out in handling them, because it cannot always be foretold when the patient will become sputum positive and infect his highly susceptible associates. 2. There is much to be gained in gastric lavage in primary tuberculosis. It is true that many times few bacilli are present, and they may be found only on culture and guinea pig inoculation, but it is a worth while procedure. Before the advent of antibiotic therapy and chemotherapy, Paulson found that in the average primary tuberculous infection tests remained positive for about three years. Now the time is much shorter, but the presence of tubercle bacilli in the gastric secretions is evidence of continuing activity of the disease, although it may appear healed. The finding of bacilli in gastric secretions does not always mean the child will infect others. Unless bacilli are found in the sputum or throat swabs, the possibility of infecting others is extremely unlikely. 3. While there are exceptions to all rules, there would generally be expected to be a decided difference in the infectivity of the two children. The one without roentgenographic changes would most likely have negative sputum and gastric secretions, while the other, during the active phase of the disease, would have positive gastric secretion and may have positive sputum or throat swabs and thus would be infectious. It may happen rarely that an open lesion will exist behind the heart or in the "invisible" areas of roentgenograms of the lungs, in which event the secretions will be positive. 4. The first child may remain in the orphanage so long as he does not show signs of clinical disease, roentgenographic evidence of clinical disease, and, especially, positive mouth or gastric secretions. He should be examined monthly, for several months, until presence of the infection is proved or disproved, and action should be governed accordingly. The second child should be removed if his mouth secretions are positive and should be given drug therapy, which should render his secretions negative and safe in a few months, after which he may be returned to the orphanage. 5. There is no good evidence that rest is beneficial in primary tuberculosis. Rest as applied to active adult disease is not necessary. During any active or febrile phase of primary diseases, as much rest is recommended as can be had, but when the patient becomes symptom-free rest has been found unnecessary. This latter fact was established by Myers, in Minneapolis, when he closed the Lymanhurst Institution. The child should not, however, become fatigued, and good hygienic measures should be followed. It is better to treat such a child as an outpatient. 6. Lumbar puncture is liable to do more harm than good, as the questioner suggests. Besides, the chances of finding positive cases so early in meningitis are so remote it would be an utter waste of time.

CARE OF THE HAIR

To the Editor:—*How often should one's hair be shampooed? Of what value are detergents? I hear so much about different brands, yet I am hopelessly mired in ignorance. Is there any harm in putting water on the hair when grooming it?*

M.D., California.

Answer.—Washing the hair per se will not result in hair damage but if strong cleansing agents are consistently used, the hair and scalp may become excessively dry. Years ago, cleansing agents were often more alkaline than they are today, and inferior shampooing results were not rare. There are few persons who find it necessary to wash the hair more than twice a week. The average person in a city may require shampoos once a week. Wetting the hair for grooming purposes is not harmful. The type of detergent used in a particular shampoo is a trade secret, unless the manufacturer wishes to disclose it. Some shampoos contain both a soap and a synthetic detergent product. The most satisfactory criterion for determining shampoo action is to experiment with several reputable brands until one is found that suits the individual needs. This experimentation will not result in serious hair damage. The most that will occur is temporary excessive dryness and such cosmetic disadvantages as inferior manageability and hair gloss. In general, synthetic detergents are efficient cleansers, and some would not be suitable for any but extremely oily hair; however, by the addition of certain chemicals, cleansing ability can be decreased, and a product can be produced that is satisfactory for dry and average hair. When excessive dryness of the hair persists despite a change in shampoos, other causes should be investigated. Over-processing during permanent waving is a common cause of brittleness and dryness of hair. The possibility of organic causes also should be ruled out.

NEUROFIBROMATOSIS

To the Editor.—*Today I saw a 29-year-old woman with what undoubtedly is neurofibromatosis. I biopsied a lesion several years ago. Her affliction started about 12 years ago, and she is covered with hundreds of these lesions. Her face is pitiful. It has been my impression that surgical removal of the lesion, which actually causes pain, is about the only treatment recommended. Would there be any merit in considering the use of an estrogenic hormone? Since corticotropin (ACTH) or cortisone has been tried in every other known affliction, have these preparations been used in this disease?*

M.D., Alabama.

Answer.—Neurofibromatosis (Recklinghausen's disease) starts before the age of 17 or 18 and usually makes its first appearance in early childhood, although it may reach its peak when the patient is in his twenties. Surgical removal of the painful lesions is the most satisfactory method of treatment. There is no reason to believe that corticotropin or cortisone would be of any value. Other hormones used in the past in the treatment of this disease have had no effect.

REPEATED ATTACKS OF ERYTHEMA NODOSUM

To the Editor:—*A married man, aged 38, has a history of vivax malaria, colitis of many years duration, and repeated attacks of erythema nodosum. At the age of 34, while at rest, he felt a hypesthesia involving the right face and arm, which subsided after an hour; at the time he had erythema nodosum. In 1952, after a healthy four years, he had a severe supraorbital headache, an unnatural feeling of extreme fatigue, and difficulty in walking properly and in writing. This gradually subsided in a day or two, with complete recovery. In December of the same year, again following strenuous work and sleeplessness, he had the same headache with extreme fatigue, but this time he noted a short-lasting diplopia involving the right rectus lateralis. Results of physical examination during and after the attack, blood cell counts, and serologic tests for syphilis have been negative. Roentgenograms of the skull are not contributory. I would appreciate your opinion on diagnosis and management in this case.*

M.D., Lebanon.

Answer.—Erythema nodosum is a symptom complex, not a specific disease entity. It may be a manifestation of any of the following conditions: ingestion of such drugs as iodides, bromides, or sulfonamides, endocarditis, arthritis, recurrent septic sore throats, rheumatic fever, tuberculosis, leprosy, syphilis, malaria, trypanosomiasis, venereal lymphogranuloma, chancroid, acute exanthemas, Neisseria infections, typhus fever, Boeck's sarcoid, fungus infections, and, frequently, infection with intestinal parasites. The history of the patient in question, while lacking in many specific details, gives some highly suggestive points of approach, namely, youth, a history of vivax malaria, stubborn colitis, and repeated attacks of erythema nodosum, some early symptoms of a vascular or nervous nature, fleeting hypesthesia, impaired locomotion and ability to write, and short-lasting diplopia. All of these episodes followed extreme physical fatigue and sleeplessness. A chronic cerebral malarial infection would produce any of the above symptoms, individually or grouped. In this type, the blood is usually negative for malarial parasites. A spinal fluid examination is indicated, and would show increased pressure, up to 400 lymphocytes per cubic centimeter, abnormally high albumin and globulin levels, and also, sometimes, pigments from malarial parasites. Meningism may be the cause of diplopia. The colitis could be a manifestation of an abdominal type of malaria. Undulant fever should be eliminated by means of a Brucellergen (a suspensoid of protein nucleate derived from Brucella organisms) test. Roentgenographic examination for internal Boeck's sarcoid and a more complete history, including information on episodes of fever, travels, and diseases endemic in the environment of this person, would help. No opinion about management has any value until a definite diagnosis has been established.

OCCUPATIONAL THERAPY IN EARLY RHEUMATOID ARTHRITIS

To the Editor:—*In an early stage of rheumatoid arthritis when the joints of fingers, hands, and wrists are becoming swollen, painful, and stiff, is playing the piano a helpful exercise? Can it be recommended as a pleasant substitute for the usual exercises, which are exercises and nothing more?*

M.D., Texas.

Answer.—Carefully planned occupational therapy may not be entirely satisfactory as a substitute for exercises in rheumatoid arthritis, but occupational therapy has the great advantage of minimizing the monotony and boredom that may accompany performance of calisthenic-like exercises. Physicians who plan occupational therapy for patients with rheumatoid arthritis should keep in mind certain objectives: the activity should consist of work that is interesting, the work chosen should entail articular and muscular movements calculated to maintain and improve action of affected joints, and the work involved should not cause excessive fatigue. Occupational therapy that is properly planned may serve an important function in ridding patients of feelings of helplessness and dependency. Playing the piano may serve well as occupational therapy for rheumatoid arthritis involving fingers, hands, and wrists. The duration of practice should be supervised and should depend upon the character of the disease. If the process is active and swelling is pronounced, 10 or 15 minutes should suffice. If the disease is relatively inactive, the amount of time devoted to practice can be prolonged.

INTRAUTERINE FETAL DEATH

To the Editor:—*A 22-year-old woman is married to a third cousin. Her mother and father-in-law are first cousins. Her blood is type B, Rh-negative, and her husband's blood is type AB Rh-negative. About one and one-half years ago, she gave birth to a 3¾ lb. (1,701 gm.) boy one week after expected confinement. The infant lived only a few hours. The placenta was said to be normal. Autopsy revealed no apparent cause of death. In December, 1952, after a second uneventful pregnancy, she noted a cessation of fetal movements at the onset of labor. A dead, macerated female fetus, weighing less than 4 lb. (1,814 gm.) was delivered about eight hours later. Three infarcts were noted in the placenta. Autopsy again revealed no apparent cause of death. The patient's blood pressure ranged between 120/80 and 142/90 throughout the pregnancy. At no time was albuminuria, pyuria, or glycosuria noted. The results of the Mazzini test were negative. The patient's weight gain was normal. What would cause these fetal deaths and the infarcts noted in the second pregnancy? Should this woman attempt to conceive again, and, if so, should a cesarean section be done about two weeks before expected term in the hope of getting a viable child?*

M.D., New York.

Answer.—Little information is available concerning the factors that predispose to intrauterine fetal death, with or without associated infarction of the placenta, in women who do not have chronic hypertensive vascular disease. A complete study of the patient, which should include the usual kidney function tests, will rule out the latter condition. It may be well to check thyroid function by means of a blood protein-iodine determination as well as a basal metabolism test. The distant relationship of the parents is of no importance in causing the fetal deaths. The mother should be encouraged to conceive again. She should be encouraged to take a high protein diet but to restrict her weight gain to no more than 8 to 10 kg. If she has hypometabolism, she should receive thyroid. It is preferable to await a natural delivery unless toxemia should begin to develop. The small size of the fetuses may be an indication of poor nutrition because of an inadequate uteroplacental blood supply. In chronic hypertensive vascular disease the lesion is in the placental site, which leads to changes in the placenta and a decreased circulation to the fetus.

MENTAL DEPRESSION DURING MENSTRUATION

To the Editor:—*Please discuss the management of a 37-year-old woman who is greatly depressed one to two days prior to, during, and seven days following menstruation. There is no appreciable change in the menstrual cycle, and no organic disease can be found.*

George E. Quinn, M.D., Farmington, N. H.

Answer.—This patient obviously needs sympathetic psychiatric study to find the cause of her depression. There is a tendency to relate these things to the menstrual cycle when the real trouble is psychiatric. Naturally, just before the menstrual period the hormone blood levels rapidly drop, and a certain degree of letdown is understandable, but it happens in all women who menstruate and does not cause undue depression. This patient should not be treated with hormones, because, although such therapy may temporarily give slight improvement, it would not solve her basic problem and would eventually fail to give relief.

MULTIPLE POSITIVE REACTIONS TO ALLERGIC SKIN TESTS

To the Editor:—*A patient, aged 43, had no allergic manifestations until four months ago, when he received three daily injections of penicillin. Later he began to take a standard multivitamin and multimineral tablet. The list of positive reactions found by a competent allergist is enclosed. I have never seen a report with so many positive results. I am suspicious of the penicillin or the vitamin and mineral tablets. With all these allergies, the patient is kept well under control by the use of the antihistamine preparation methapyrilene hydrochloride (Histadyl). How should I proceed in this case?*

M.D., New Jersey.

Answer.—If the urticaria began several days after penicillin administration it is probably an example of the common form of the "serum sickness" type of reaction to this antibiotic. This type of urticaria or angioneurotic edema resulting from a penicillin reaction may last for hours or months or even longer than a year. Ultimately the syndrome disappears. The diagnosis is made from the clinical history and the exclusion of other possible causes of urticaria. The result of a skin test with penicillin is almost always negative in this type of allergy. Furthermore, in the majority of all types of urticaria, the skin tests are negative. Certainly the majority of positive skin tests as reported in the attached list have no bearing on the patient's complaints. There are several possible explanations for the large number of reactions. One of the most likely is the patient's skin irritability, which often occurs in urticaria. The allergy tests reported to the inquirer constitute a classical example of the many types of misapplication and misinterpretation of the skin test in allergy. Provided the timing of the onset is compatible with a history of penicillin reaction, the best advice to the patient is to disregard the syndrome, except for obtaining symptomatic relief.

FUNGUS INFECTION OF NAILS

To the Editor:—*A friend has a fungus infection of all the nails on one hand. He has consulted dermatologists, none of whom had any satisfactory treatment. The nail bed is being replaced by irregular, white, raised, dry areas, which become piled up unless they are scraped down. Has plastic surgery been tried? If so, please describe this method.*

M.D., Arkansas.

Answer.—It would be desirable to isolate and identify the causative organism in this case. Such identification might give a better idea of the prognosis, because new fungicides and new keratolytic vehicles are constantly being introduced for which claims for specificity are made. All such drugs should be tried before resorting to surgical avulsion, because the results from surgery are too often unsatisfactory. If the nails are removed by surgery, the nail bed and matrix must be treated thoroughly and continuously with fungicides.

SOFTENED WATER

To the Editor:—*Is there any danger in using water softened by ordinary commercial softeners for drinking or cooking purposes? Is there any benefit? Does such water have any effect on nutritive value of cooked foods?*

Arthur W. Anderson, M.D., Lexington, Neb.

Answer.—Any proper water softening is without significant physiological import. The advantages of softened water chiefly are economic, relating to such matters as laundering, hair washing, conservation of detergents, cleanliness of plumbing fixtures, and taste and appearance of food. Some hard waters modify the appearance of tea and the flavor of coffee. It is true that well-softened waters employed in cooking extract a higher percentage of the minerals of vegetables and possibly of the vitamins, but this is not characteristic of ordinary chemically softened waters. In general, it may not be claimed that softened waters introduce physiological detriment, and the advantages far outweigh any usual objections.

CHOLINE AND METHYLENE BLUE

To the Editor:—*Is the use of choline 5 grains (0.32 gm.), in 1 oz. (30 cc.) of an alkaline eye wash solution contraindicated? Is the use of methylene blue, in a proportion of 1/150 grain (0.4 mg.) per 8 oz. (250 cc.) of alkaline eye wash solution contraindicated when choline is included in the solution? Does choline have the power of inducing penetration in the deep structures of the eye coats if methylene blue is included in the proportions mentioned, and is there any possibility of permanent stain in these structures? Will methylene blue in such proportions have antiseptic or germicidal properties of value?*

Vincent Boccella, M.D., Glenside, Pa.

Answer.—Choline, a viscid, strongly alkaline liquid, is commercially available, but the salts are usually used, the most popular forms being choline chloride and the more stable choline dihydrogen citrate. The bicarbonate and borate salts are also obtainable. In 1% solution, choline bicarbonate is slightly alkaline and choline dihydrogen tartrate slightly acid. Either could be used in the eye wash, the choice depending on the final pH desired. Methylene blue is easily salted out of solution and, hence, is considered unsuitable for coloring solutions of salts. The suggestion that choline can induce penetration in the deep structures of the eye coats, originally proposed by Dmitry, has not received experimental support. In any case, no permanent stain can result from the use of methylene blue, as the compound is rapidly reduced in the tissues to the colorless form. Although methylene blue is antiseptic for pure cultures in 1:150,000 dilution, the proposed eye wash would have three times this dilution. Methylene blue is a slow-acting, weak germicide, and, in the colorless form, it is inert.

GIANT CELL TUMOR OF FEMUR

To the Editor:—*Please advise me concerning a benign giant cell tumor of the distal end of the femur. What are the advantages of amputation and the possibility of eventual metastasis if amputation is done, even though the tumor is considered benign at present?*

Louise M. Puglise, M.D., Brooklyn.

Answer.—The treatment of benign giant cell tumor of the distal end of the femur may be carried out in one of two ways. The area may be exposed to doses of roentgen rays given through several portals with protection of the bone by crutches or splint to prevent pathological fracture, or the lesion may be removed by thorough curettage and the use of an escharotic, such as zinc chloride solution, followed by packing with bone chips and primary closure of the wound. In the surgical treatment of giant cell tumor, it is essential that the complete removal be done at the first operation and that primary wound healing be obtained. Amputation should be confined to cases in which there has been evidence of a transformation to malignant giant cell tumor or cases in which wound infection and fungation precludes satisfactory management by any other method. Such a surgical complication nowadays is seldom encountered. The possibility of metastasis as a late complication after amputation in a tumor that is histologically benign is exceedingly remote, and the life expectation of a person who has had an amputation while the lesion is histologically benign should not be adversely affected.

TESTS FOR LIVER DAMAGE

To the Editor:—*How long must complete extrahepatic obstruction of a normal liver be present to produce enough hepatocellular changes to be manifested by abnormal cephalin-cholesterol flocculation and thymol turbidity?*

M.D., Tennessee.

Answer.—Abnormal cephalin-cholesterol flocculation and abnormal results in other tests for hepatocellular damage usually become apparent within a few weeks after complete extrahepatic obstruction of the biliary tract. Therefore, results of these tests will usually be normal during the first week or two. This is of value in differential diagnosis between an obstruction and acute hepatitis.

USE OF ANTICHOLINGERIC DRUGS IN PEPTIC ULCER

To the Editor:—*A recent news item described a substance designated BA-5473, which was reportedly effective in the management of peptic ulcers. My patient has a large ulcer and is interested in trying this drug. Kindly inform me whether the news item was correct and where the drug is available.* *Millard Pasthuma, M.D., Cadillac, Mich.*

Answer.—Shortly after the demonstration by Dragstedt and his associates that gastric vagotomy had a beneficial effect on the healing of duodenal ulcers, attempts were made to produce medical vagotomy by means of drugs that would depress or paralyze the vagus nerve endings in the stomach. Several such anticholingeric drugs are now available, and they exert a depressant action on the nervous mechanism of gastric secretion without producing side-effects that are prohibitive. Some of the newer drugs depress gastric secretion even after the vagus nerves to the stomach have been divided and so may be said to have a true antisecretory action. At present, until more extensive clinical trial has been made, it is wise to use these preparations as adjuvants to the standard type of medical management employing alkalies and frequent feeding. BA-5473, or Antrenyl (oxyphenonium bromide), manufactured by Ciba Pharmaceutical Products, Inc., of Summit, N. J., is one of these preparations.

MULTIPLE OSTEOMAS OF SKULL

To the Editor:—*I should like information about treatment of multiple osteomas of the skull in a 25-year-old woman. They have been present for at least 10 years, are slowly progressing in size, and so far have produced no neurological changes. The largest one is in the center of the forehead and causes a noticeable deformity, which is becoming a psychological problem. The roentgenographic appearance shows dense bony tumors that extend inside the cranial vault. Would it be possible to improve the patient's appearance by making an incision from above the hairline and trimming off the osteoma flush with the normal plane of the forehead?* *M.D., Washington.*

Answer.—From the description, this is an unusual case. There is not sufficient detailed information given to make a diagnosis. Multiple osteomas are seldom seen. If the tumors in this case extend intracranially they would not appear to be ordinary osteomas. They may possibly be meningiomas. In making a diagnosis in this case, roentgenograms should be of considerable assistance and ought to be interpreted by a competent roentgenologist. If the tumor extends intracranially, it probably should be removed along with the inner table of the skull with a tantellum plate used for replacement. If the tumor extends into the region of the longitudinal sinus, this would have to be taken into consideration.

GLASS IN INTESTINAL TRACT

To the Editor:—*A patient swallowed some glass that was in the bottom of a soft drink bottle in August, 1952. 1. How long can the glass remain in the intestinal tract without penetrating the wall and without being expelled in the feces? 2. Can the glass penetrate the wall of the intestinal tract without producing noticeable peritonitis? 3. If a small portion of the glass penetrates the wall of the intestinal tract, what is the possibility of it subsequently traveling to a remote vital organ and causing damage there?* *M.D., Georgia.*

Answer.—1. Glass, unless it becomes attached to the bowel wall, passes normally through the digestive tract surrounded by feces. 2. Glass penetrating through the intestinal wall produces local or generalized peritonitis. 3. A spicule of glass may travel like a needle and penetrate a distant organ in the abdomen. Some pieces of glass are radio-opaque and may be seen roentgenographically.

POLYPS IN THE DUODENUM

To the Editor:—*A roentgenologist has observed a polyp in the first portion of the duodenum of a woman who has no gastrointestinal symptoms. Do such polyps ever become malignant? What is the consensus regarding their removal?* *L. R. Evans, M.D., Laramie, Wyo.*

Answer.—Polyps in the first portion of the duodenum are relatively rare. If they are sessile polyps and are on a long pedicle, they may cause an obstruction by migrating in through the pyloric canal. Their relation to malignancy has been questioned by many workers; however, they should be removed, because of the possibility of the occurrence of obstructive manifestations and interference with the normal motility of the duodenum and because they have a great tendency to become ulcerated. Profuse bleeding may ensue. Air bubbles in the duodenal bulb often simulate polyps in roentgenograms. Present day fluoroscopic compression techniques disperse this air so that such errors in diagnosis now occur less frequently.

TUBERCULOSIS IN YOUNG CHILD

To the Editor:—*In October, 1950, a 17-month-old child was found to have pulmonary miliary tuberculosis. He was given thiazolsulfone (Promizole) and 1 gm. of streptomycin daily for five months. Streptomycin therapy was discontinued, and thiazolsulfone alone has been given up to the present. The chest roentgenogram has remained stable since June, 1951; the sedimentation rate, the white blood cell count, and the differential count have been normal since January, 1952. The child has had no fever during this period and is eating well and gaining weight. Can you advise from these meager details whether thiazolsulfone therapy should be discontinued? Should withdrawal be abrupt or gradual?* *B. F. Grotts, M.D., Michigan City, Ind.*

Answer.—The principal danger facing the patient with arrested miliary tuberculosis is tuberculous meningitis. When meningitis occurs, it usually develops within the first year following arrest of the disease by the use of specific drugs. It appears probable that, since two years have elapsed in the case described, adequate treatment has been given.

SMALLPOX VACCINATION OF INFANT

To the Editor:—*A 3-month-old healthy male infant has had three smallpox vaccinations with vaccine of a standard make and has never shown any reaction. The mother was vaccinated when she was a baby; she is now 23 years old. I have never seen such a case. When should smallpox vaccination be attempted again?* *Eugene M. Kistler, M.D., Allentown, Pa.*

Answer.—Inherited immunity to smallpox often persists in an infant for six months or longer, provided the mother has had a successful vaccination. This probably is the reason for the failure to obtain a successful vaccination in the first three attempts. An attempt should be made after three more months have elapsed.

ICHTHYOSIS

To the Editor:—*A girl, 11 years old, has ichthyosis and, in addition, teeth that are poorly formed, yellow, and pitted. She has a low basal metabolism and has been taking 1 grain (0.06 gm.) of thyroid three times a day along with Maltine with cod liver oil and creosote. She eats well and drinks adequate amounts of milk. Have you any suggestions?* *Watson B. Morris, M.D., Springfield, N. J.*

Answer.—Ichthyosis is a congenital abnormality. A specific cause has not been established. Mild cases sometimes clear up spontaneously at puberty, and in some cases the administration of vitamin A seems to be effective. A soft ointment containing 2% salicylic acid is usually helpful. The changes in the teeth may be independent of the cutaneous disorder.

AIR EMBOLISM FOLLOWING ARTIFICIAL PNEUMOTHORAX

TO THE EDITOR:—*In* THE JOURNAL, *May 16, 1953, page 293, is a discussion of air embolism following artificial pneumothorax, in which it is said that nothing can be done for this type of air embolism except to hope that it does not reach a vital center. Cases are on record in which the immediate change of the patient's position to the left lateral recumbent or the Trendelenburg position, which permits trapping of the air bubble above the blood in the right ventricle, has enabled the observer to aspirate air directly from the right ventricle. Such a procedure was reported by Stallworth, Martin, and Postlethwait in* THE JOURNAL (**143**:*1250 [Aug. 5] 1950).*

William B. Bean, M.D.
State University of Iowa, Iowa City.

TO THE EDITOR:—*The answer to the query on air embolism following artificial pneumothorax in* THE JOURNAL *May 16, page 293, is misleading, probably because the query is misunderstood. The query relates an incident of air embolism to the right ventricle following refill of an extrapleural pneumothorax. In the answer air embolism occurring in intrapleural pneumothorax is discussed. Air embolism from extrapleural pneumothorax usually does not result from a bronchovenous fistula, as occurs in the case of intrapleural pneumothorax. It is probable that a systemic vein was lacerated in this case so that air already present in the extrapleural pneumothorax space was able to enter the venous return to the heart and obstruct blood flow to the lungs from the right ventricle. Death was due, therefore, to forward cardiac failure and peripheral ischemia rather than to air embolism to the coronary arteries or centers of respiration in the brain. The latter could occur only if there was a congenital opening between the two sides of the heart so that air entering the right chambers could cross into the left chambers and then proceed to the peripheral circulation. The treatment the California doctor used was correct; he turned the patient on the left side hoping that an air trap in the outflow tract of the right ventricle would be relieved, since in the left decubitus position the outflow tract is inferior to the rest of the right ventricle and the air would rise out of the outflow tract. The principle involved has been studied by Dr. Thomas Durant and his associates* (Am. Heart J. **33**:*269, 1947;* Pennsylvania M. J. **56**:*279, 1953). It is possible to prevent death in such cases, if the amount of air entering the right ventricle is not excessive.*

I take exception to the statement, "The accident should never happen if the technique is good and the cases are properly selected." Such accidents may happen regardless of how careful the operator is, because it is not possible for him to have his eye at the point of the needle so that he can see where it is going and avoid lacerating blood vessels.

William Weiss, M.D.
Philadelphia General Hospital, Philadelphia 4.

TO THE EDITOR:—*In his reply to the query on air embolism in* THE JOURNAL *for May 16, 1953, page 293, I think your authority has confused arterial and venous air embolism. The inquirer says that air was introduced into an extrapleural pneumothorax and at autopsy the right ventricle was full of air. This phenomenon was therefore due to air entering a systemic vein and reaching the right side of the heart. When the needle forms a communication between a bronchus and a pulmonary vein, air reaches the left ventricle and causes symptoms by entering the coronary arteries (death) or cerebral arteries (such as hemiplegia or visual defects). It is possible for air from the right side of the heart to reach the brain if there is a patent interauricular septum or if it passes up the internal jugular vein or traverses the paravertebral plexus of veins. Diagrams showing the routes taken by air emboli can be found in "Emergencies in Medical Practice," edited by C. Allan Birch (ed. 3, E. & S. Livingstone, Edinburgh, 1952).*

It may be added that to turn the patient on the left side is good treatment in all cases. When air is in the right ventricle, it is less likely to obstruct the outflow tract if the patient is lying on the left side. When air is in the left ventricle, it is less likely to enter a coronary artery when the patient is in this position because the part of the aorta that is uppermost does not have a coronary orifice.

C. Allan Birch, M.D.
2, Slades Hill, Enfield, England.

TREPONEMAL IMMOBILIZATION TEST

TO THE EDITOR:—*To the information on the treponemal immobilization test in* THE JOURNAL *March 14, 1953, I would like to add that the Division of Venereal Disease Control, Province of Ontario, commenced use of the Treponema pallidum immobilization test toward the end of 1951, as a service to physicians in this province. The use of the test originally was restricted largely to cases in which physicians had difficulty in interpreting the results of the standard serologic tests. Priority was given to specimens from prenatal, premarital, and preemployment subjects. The physicians of the province cooperated to such an extent that in July, 1952, the department of health of Ontario was in a position to extend this service to the remaining nine provinces of Canada as well as to the armed forces. The average number of specimens received each week rarely exceeds 100, which is the maximum capacity of the TPI unit in the central public health laboratories in Toronto. The director of the Division of Venereal Disease Control feels that the test is one more aid in resolving the difficult problem of differential diagnosis in latent syphilis. For physical and other reasons, the services of the Treponema pallidum immobilization test are provided only for the physicians of Canada, through the divisions of venereal disease control for each province.*

George W. Miller, M.D.
Assistant Director
Division of Venereal Disease Control
Department of Health
Province of Ontario, Toronto, Canada.

CONGENITAL HYDROCELE

TO THE EDITOR:—*In the Query and Minor Note on "Congenital Hydrocele" in* THE JOURNAL *Feb. 21, 1953 (page 694), it is stated, "simply closing the inguinal area off alone and leaving the distal end in situ would most likely be followed by a recurrence of hydrocele fluid accumulation." For some unknown reason, this is not true. I have treated many patients with congenital hydrocele by transecting the sac along the cord and closing the inguinal area in one way or another to prevent congenital hernia. Occasionally, I have split the distal end of the hydrocele sac lengthwise for a short distance down the cord; however, I have never removed or everted it. To my knowledge, the hydrocele has not recurred, and some of my patients have been followed closely for more than 10 years. Undoubtedly, the incidence of traumatic injury to the vas deferens is related directly to the extent of surgery performed within the scrotum. In young children, particularly, the vas deferens is very delicate in the dependent portion of the scrotum, and the chance of its occlusion by traumatic injury is probably greater than the chance of a recurrence of the hydrocele fluid if the distal end of the sac is left in situ.*

Miles Griffin, M.D.
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Oakland 9, Calif.

TUBAL LIGATION IN RH-NEGATIVE MOTHER

TO THE EDITOR:—*The answer to the query in* THE JOURNAL *May 16, 1953 (page 295), about tubal ligation in the Rh-negative mother who has had an erythroblastotic infant should be amplified. It is important that the father's Rh genotype be determined, because, if he is Rh_o heterozygous, half the progeny will be Rh negative. There are more Rh_o heterozygotes than homozygotes. The statement that tubal ligation is an entirely final procedure is, of course, true, but the family may be offered a ray of hope in the determination of the father's Rh genotype.*

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